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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 27 1953

DIABETIC MYELOPATHY

BY

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Neurological complications of diabetes mellitus have been recognized for nearly a hundred years (de Calvi, 1860) and during the present century the orthodox teaching has been that diabetes mellitus may result in a symmetrical polyneuritis expressing itself largely by tenderness of the legs, loss of knee- or ankle-jerks, ataxia, sensory loss in the feet, and perforating ulcers, constituting the picture of diabetic pseudo-tabes. Martin (1953) has said that neuropathy is "characterized by a diffuse and ill-localized pain, vasomotor disturbances, thermal paraesthesiae, changes in tendon-reflexes, and often an alteration in pain sensibility in the feet without much impairment of touch or pressure. If the disorder progresses shooting pains develop, vibration sense is lost and, lastly, sense of touch and position as well as motor power becomes involved." These statements accord well with textbook descriptions (Gowers, 1893; Collier, 1926; Brain, 1951) and are supported by the literature of the past fifty years.

Rudy and Epstein (1945), after an analysis of 100 examples of diabetic neuropathy, stated that pain and sensory disturbances were the commonest manifestations, and neither they nor Rundles (1945), in an exhaustive survey of this subject, make any mention of a purely motor form of diabetic neuropathy. Jordan (1936) and Woltman and Wilder (1929) also emphasized that the neurological changes in diabetes mellitus are mainly sensory and that motor disturbances are rare. Although there are many casual references to weakness and wasting of muscles in association with sensory disturbances, the important observations of Bruns (1890) have been overlooked or dismissed as irrelevant. He described three patients, aged 58, 59, and 70, suffering from diabetes mellitus of short duration; all three developed severe pain in the hip and thigh followed by weakness and wasting of leg muscles without objective sensory loss, and each recovered fairly quickly following dietary restriction.

The reality of diabetic neuropathy without objective sensory loss has become apparent to us from clinical observation of the following patients; the case histories are presented in the order in which the patients came to our attention.

Case 1

A man aged 56 was first seen by one of us (H. G.) on March 14, 1950. He gave a two-months history of pain in the lumbar region and down the back of the right leg to the heel and toes, with less severe pain down the back of the left leg, getting steadily worse, and numbness down the back of the thighs and calves. There was no specific complaint of weakness, but there had been polyuria and polydipsia for one year, with loss of 28 lb. (12.7 kg.) in weight. He had diffuse and severe wasting and weakness of all the muscles of the right leg, including the gluteus maximus, with loss of the right knee-jerk and both ankle-jerks. There was no sensory loss. The blood pressure was 150/80 mm. Hg. He was found to have glycosuria, and was admitted to hospital. The diabetes was well controlled by a diet of 10 black, 8 red (10B, 8R) Lawrence lines, and 10 units of zinc-protamine insulin (Z.P.I.) daily.

Investigations.—The cerebrospinal fluid (C.S.F.) protein was 68 mg. per 100 ml.; Lange 0013331000; fasting blood sugar, 350 mg. per 100 ml. Radiography of the lumbar spine was normal.

When seen again on June 8 he was still taking tab. codein. co. to relieve pain. His disability was stationary or increasing, and the left knee-jerk was now seriously depressed. On readmission to hospital on August 15 there was considerable weakness of most muscles of the left leg and he was only just able to walk. C.S.F. protein, 105 mg. per 100 ml. Lange 1233310000.

In December, 1950, both knee- and ankle-jerks were absent and the plantar responses were extensor. He did not begin to improve until early 1951; by April he could walk with one stick, and in November he was walking quite well. In May, 1952, his urine was constantly sugar-free on 12 units of Z.P.I. daily. By July he was walking very well unaided, the knee- and ankle-jerks were still absent and the right plantar response was extensor, but the left was now flexor—he said himself that there was "almost incredible improvement."

Electromyogram (D. T.)—On September 25, 1952, strength-duration curves were normal except for slight partial denervation changes in the right tibialis anticus muscle. Needle electrodes in both tibialis anticus and quadriceps muscles showed a decreased sustained pattern of motor-unit activity on voluntary contraction, with prominent single units superimposed, which in places amounted to discrete motor-unit activity. There was no spontaneous activity.

In January, 1953, there was only a little aching in the legs. He was walking quite well without sticks and was just able to jump off the ground. There was no demonstrable weakness or wasting of leg muscles and tone was normal. The knee-jerks were just present, but the ankle-jerks were still absent. The plantar responses were both flexor. There was no sensory loss. The diabetes was fully controlled, and he had gained 50 lb. (22.7 kg.) in weight.

Case 2

A man aged 63 was first seen by one of us (H. G.) on June 1, 1950. There had been pain in the left buttock, radiating down both back and front of the left leg to the ankle only, for two months. The pain was improving and

was said to be better when walking. The leg felt generally weak and he had fallen several times. There were no symptoms in the right leg. He claimed to have known that his knee-jerks had been absent all his life. There was patchy weakness and wasting of the left leg muscles, with depression of the left ankle-jerk and absent knee-jerks. He could walk only with a stick and was quite unable to jump off the ground. There was no sensory loss. He was admitted to hospital and found to have glycosuria.

Investigations.—The glucose-tolerance test showed impaired sugar tolerance. The C.S.F. protein was 139 mg. per 100 ml.

Treatment was begun with a 14B 9R Lawrence line diet together with 20 units of soluble insulin and 20 units of Z.P.I. daily, which was later reduced to 16 units of soluble and 16 units of Z.P.I. daily. He was fitted with a left toe-raising spring.

He began to improve rapidly, and by September had gained 14 lb. (6.4 kg.) in weight. On January 25, 1951, he was able to hop on one foot, and in April his insulin dosage was reduced by half.

Electromyogram (D. T.).—On September 18, 1952, strength-duration curves from both quadriceps and both gastrocnemii showed slight partial denervation. Needle electrodes in these muscles revealed irregular spontaneous motor-unit activity which was polyphasic in places. On voluntary contraction the motor-unit pattern was decreased, but superimposed isolated motor units gave an appearance approximating to that of discrete motor-unit activity.

When he was last seen, on February 19, 1953, the diabetes was controlled and the weight steady, though there was still some aching pain in the legs. The knee-jerks were absent, but the ankle-jerks were brisk; there was little weakness and he was walking normally.

Comment.—It was felt at this stage that both this patient and Case 1 were examples of a diabetic neuropathy of an unfamiliar type.

Case 3

A man aged 58 was seen by one of us (H. G.) in July, 1952, and diagnosed as another example of diabetic neuropathy similar to Cases 1 and 2. He had been attending a diabetic clinic for nearly two years, and at various times had been diagnosed as suffering from sciatica or motor neurone disease, with auricular fibrillation and hepatomegaly. In 1948 he developed a left external rectus palsy which recovered in six months. During 1950 he slowly developed pain in the right hip and down the right thigh to the knee, which was worse on walking but was unaffected by coughing. Early in 1951 he noticed polyuria and polydipsia, and glycosuria was detected. He became slowly worse, and by the spring of 1952 he could not walk more than 100 yards without a stick; in July he was unable to stand or sit up without help. There was weakness and wasting of the spinal muscles, with diffuse weakness and wasting of the legs, especially the right quadriceps, and some fasciculation of the left quadriceps. The knee- and ankle-jerks were absent. There was no sensory loss. The blood pressure was 105/60 mm. Hg.

Investigations.—The C.S.F. protein was 109 mg. per 100 ml.; Lange 0001210000; glucose-tolerance test showed evidence of impaired tolerance.

He was then admitted to Pinderfields Hospital, Wakefield, and given a 16B 8R Lawrence line diet and 10 units of Z.P.I. daily, together with suitable active physiotherapy. He began to improve rapidly.

Electromyogram (D. T.).—The patient was examined on three occasions during the second half of 1952. Strength-duration curves revealed widespread partial denervation of the leg muscles. Needle electrodes showed scanty fibrillation activity and widespread spontaneous motor-unit activity, often polyphasic in type, in the leg muscles. On voluntary contraction there was discrete motor-unit activity in the tibialis anticus (Fig. 1) and quadriceps muscles on both sides, but the surviving motor-units were of normal amplitude. A short burst of low-frequency repetitive activity was detected in the left tibialis anticus muscle. In November, 1952, there was definite improvement in the electrical activity of the affected muscles.

On November 3 he was free from pain and gaining weight, and the urine was sugar-free. There was slight diffuse weakness of both legs with wasting, especially of the thighs, marked hypotonia, and absent knee- and ankle-jerks. Fasciculation was no longer apparent. He was just able to jump off the ground. On December 29 he could hop on his left foot, and the ankle-jerks were brisk. On February 23, 1953, there was still wasting of the thighs and calves, more marked on the left than the right, with slight weakness of all leg muscles. The right knee-jerk had returned and the plantar

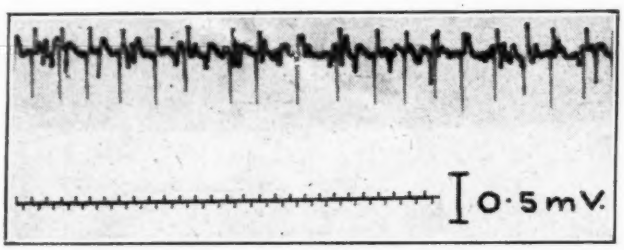

FIG. 1.—Record of electrical activity during full voluntary contraction of the right tibialis anticus muscle of Case 3 (concentric needle electrode). Note the large discrete motor units standing out from a background showing little activity. Time: 10 msec.

responses were now extensor. Auricular fibrillation was still present, but was controlled. When last seen, on April 20, his condition was stationary and there was still no objective sensory loss.

Case 4

A woman aged 60 was first seen by one of us (D. T.) on October 5, 1952. There was a three-months history of severe aching pain radiating down the back of the left thigh and leg from the buttock to the outer malleolus and toes, worse when resting but unaffected by coughing or straining, and a two-months history of weakness of the left leg, causing her to fall several times. She had noticed polyuria and polydipsia for six months. There was slight wasting and marked weakness of the rotators and flexors of the left hip, left quadriceps, and extensors of the left foot and toes. The wasting was difficult to estimate because of obesity, but the left thigh diameter was 1½ in. (3.8 cm.) less than the right, and the left calf 1 in. (2.5 cm.) less than the right. There was no sensory impairment. The right knee-jerk was brisk, the left absent, the ankle-jerks were sluggish, and the plantar reflexes were flexor. The urine contained sugar but no acetone.

Investigations.—Radiography of the lumbar spine was normal. On October 10 the C.S.F. protein was 34 mg. per 100 ml. The glucose-tolerance test on October 13 showed impaired sugar tolerance.

Electromyogram (D. T.)—On October 17 the left quadriceps and left tibialis anticus muscles showed a greatly decreased pattern of motor-unit activity on voluntary contraction. Large isolated motor units were superimposed on this background activity, giving a picture approximating to discrete motor-unit activity. Similar but less marked changes were found in the right quadriceps and tibialis anticus muscles. There was no spontaneous activity.

The diabetes was controlled with a diet of 12B 8R Lawrence lines and 30 units of soluble insulin twice daily. She was given remedial exercises and improved steadily on this regime. On January 12, 1953, the pain, weakness, and wasting were less marked. Both knee-jerks and the left ankle-jerk were absent; the right ankle-jerk was just present. The plantar responses had become extensor. She was just able to jump off the ground. On February 14 she had improved still further. The pain was now slight and she could walk more easily. The physical signs were unchanged and the diabetes was under control. When last

seen, on April 16, she was still improving. The right knee-jerk was absent, but the left knee-jerk and both ankle-jerks were present. The plantar responses were still extensor, and there was no objective sensory disturbance.

Case 5

A man aged 73 was seen by one of us (H. G.) on November 9, 1952, at Scunthorpe at the request of Dr. Derek Millar. The history was unreliable, but the patient had noticed white stains on his shoes after micturition during the winter of 1951. Glycosuria had been detected by his general practitioner in the spring of 1952, but no therapeutic action had been taken until August, 1952, when he had been admitted to the Scunthorpe Memorial Hospital for stabilization. On admission he had ketonuria, which rapidly disappeared with a diet of 2,000 calories and the daily injection of 10 units of Z.P.I. His urine remained sugar-free, and numerous blood-sugar estimations varied from 120 to 168 mg. per 100 ml.

During the summer of 1952 the patient began to complain of pain about the left knee, with steady deterioration of gait, which was more pronounced on the left side than on the right. When seen in November he complained of diffuse pain in the left leg, excluding the foot, which was unaffected by posture; the pain was thought to be causing insomnia. He said that in 1944 he had had a precisely similar attack, but restricted to the right leg; at that time there was foot-drop with absent knee- and ankle-jerks, but no diagnosis was made and no investigations were performed. At first he could walk only with a calliper and crutches, but he slowly recovered during the next three years. All the tendon jerks in the legs had returned by August, 1952. He said that two of his brothers, aged 29 and 49, had died of diabetes in the pre-insulin days. Simple tests suggested early senile dementia. There was slight wasting of the left thigh and calf. Muscle-testing in the left leg was handicapped by pain, but there was unequivocal weakness of all muscles of the left thigh and normal power below the left knee. There was slight weakness of all muscles below the right knee. The left knee-jerk was absent, but the other tendon-jerks in the legs were present. The plantar responses were equivocal. There was no sensory loss, tenderness, or fasciculation. The blood pressure was 150/80 mm. Hg.

Investigations.—The C.S.F. protein was 120 mg. per 100 ml. The blood-sugar level was never higher than 168 mg. per 100 ml.

The patient refused further investigation and treatment. In January, 1953, his condition was stated to be about the same.

Comment.—It was felt that this was the fifth example of diabetic neuropathy without objective sensory loss; an important feature was the earlier history, which strongly suggested a previous attack between 1944 and 1947.

Discussion

It seems fairly certain that these five patients were suffering from the same syndrome. The youngest was 56 and the oldest 73. They all had diabetes of relatively short duration, varying from three years to six months. Although some had lost a great deal of weight and all showed impairment of glucose tolerance, none had very high blood-sugar levels or had ever been in coma. None had been treated with insulin before the onset of the neuropathy, although one had been under the supervision of a diabetic clinic. When first seen the duration of the neuropathy varied from one to fifteen months. All complained of pain in the legs, usually severe, always asymmetrical, and sometimes unilateral. The pain, though diffuse, tended to be maximal in the hip and thigh. All showed some degree of wasting of the leg muscles and loss of the tendon reflexes in the legs, again patchy and asymmetrical. At some stage three (Cases 1, 3, and 4) showed unequivocal extensor plantar responses, and in a fourth (Case 5) they were doubtful. In none was there any objective sensory disturbance, tenderness, or perforating ulcers. In spite of their ages it was striking that all had normal vibration sense at the ankles. In all the patients the blood pressure was within normal limits. Four of them showed a high protein level in the C.S.F.

In the four patients on whom electromyography was performed a similar and severe abnormality was found. Strength-duration curves showed varying degrees of partial denervation of the leg muscles. There was some spontaneous motor-unit activity, but a striking absence of fibrillation potentials except in Case 2, and here they were scanty. There was a decreased pattern of motor-unit activity on voluntary contraction which amounted to discrete motor-unit activity in many areas. It is thought that these findings are compatible with, although certainly not diagnostic of, a cord lesion. They are unlike the usual

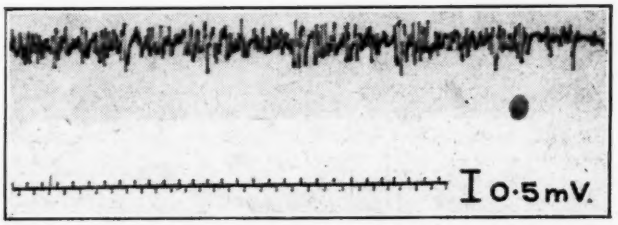

FIG. 2.—Record of electrical activity during full voluntary contraction of the left gastrocnemius muscle of a diabetic woman aged 65, with the typical clinical manifestations of polyneuritis (concentric needle electrode). Note the decreased but still sustained pattern of motor-unit activity and short duration and low amplitude of the individual motor units. Time: 10 msec.

findings in peripheral neuritis (Richardson, 1952), and bear no resemblance to the changes seen by one of us (D. T.) in other patients suffering from diabetic neuropathy of the recognized pattern (see Fig. 2). Here there is evidence of widespread denervation of the affected muscles with profuse fibrillation activity. The motor-unit pattern on voluntary contraction is well sustained, but there is a reduction in the amplitude and duration of the motor units.

Each patient was at once treated by means of a suitable diet, insulin, and active physiotherapy. Case 1 continued to deteriorate for some months, but ultimately made a complete recovery; Case 5, the oldest and least co-operative, showed no change at the time of writing, four months after he was first seen; the other three improved rapidly after the institution of treatment.

It is clear that the five cases we have described are identical with those recorded by Bruns (1890), and one of them (Case 5) had previously had a similar attack with spontaneous recovery, a point also noted by Bruns. The only important difference was that his patients recovered on dietary restriction alone, although this would no doubt be more drastic than is the practice to-day. It seems possible, however, that the natural history of this syndrome is one of spontaneous improvement, irrespective of the treatment employed. In Cases 2 and 3 improvement coincided with the institution of thorough control of the diabetes, but in Case 1 the condition deteriorated steadily for nearly a year, in spite of good control of the diabetes. The role of physiotherapy is also difficult to assess, but it would appear that vigorous active physiotherapy is of value, at any rate once spontaneous improvement has begun. It was noteworthy that considerable functional recovery could occur while the physical signs persisted unchanged or even deteriorated.

The peripheral site of the lesion in diabetic neuropathy has apparently been tacitly accepted for many years, but there are a number of references to cord lesions in the literature. Chromatolysis of anterior horn cells and degenerative changes in the posterior roots are mentioned by Courville (1945). Griggs and Olsen (1937) found degenerative lesions of the posterior and lateral columns in the cervical and mid-thoracic regions of the spinal cord. The most extensive modern study was reported by Woltman and Wilder (1929). In addition to changes in peripheral nerve fibres and the intraneural vessels they found

degeneration of the posterior columns and anterior horn cells in the spinal cords from three diabetic patients. Similar changes were described by numerous investigators at the turn of the century (Pryce, 1893; Nonne, 1896; Marinesco, 1903; Williamson, 1904; Bramwell, 1907).

Pathological studies have not been possible on the present series of patients, but there are clinical features which suggest that lesions may be present in their spinal cords. Not only is the disturbance limited to motor function but the distribution of the affected muscles is not compatible with the known distribution of peripheral nerves or nerve roots. The presence of extensor plantar responses in three, perhaps four, of the patients is unequivocal evidence of a central lesion. It is noteworthy that the plantar responses became extensor while the patients were under observation and were being treated. In Case 1 they became flexor again after some months. It may well be that the cord changes are secondary to atheromatous degeneration of the spinal arteries, but the patients all had normal blood pressures and there was no clinical evidence of arterial degeneration in their fundi or limbs. In this connexion the duration of the diabetes is probably of little importance. In the present series this has varied from six months to three years, calculated on the basis of the length of history of diabetic symptoms. This method, although obligatory, is probably fallacious in the case of middle-aged mild diabetics, and the duration of the disease may well be longer in our series (cf. Case 5). It seems to be agreed that the symptoms of the "classical" diabetic neuropathy usually develop in diabetes of long standing (Rundles, 1945), but this is not invariable. In Jordan's (1936) series of 120 diabetic patients with severe "neuritis" the condition preceded the onset of diabetes in 4, was coincident in 7, and in 28 developed within a year of the onset of diabetes.

Whatever the nature and cause of the lesion in these patients we feel that the existence of motor disturbances without objective sensory loss in diabetics, as described by Bruns over 60 years ago, is a fact of clinical importance. These patients are being misdiagnosed as suffering from other, often more serious, neurological conditions.

Summary

Attention is drawn to a form of diabetic neuropathy previously described 60 years ago but forgotten.

The syndrome consists of asymmetrical pain, weakness, muscle-wasting, and areflexia in the legs, without objective sensory disturbance, in middle-aged patients with diabetes mellitus of relatively short duration. The protein content of the C.S.F. is usually raised.

The plantar responses are often extensor and the electromyographic changes in the affected muscles are compatible with a myelopathic lesion.

Five new examples of the syndrome are described and the literature is reviewed.

REFERENCES

Bramwell, B. (1907). *Clin. Stud.*, 5, 279.
Brain, W. R. (1951). *Diseases of the Nervous System*, 4th ed. Oxford Univ. Press, London.
Bruns, L. (1890). *Berl. klin. Wschr.*, 27, 509.
Calvi, M. de (1860). Quoted by Rundles (1945).
Collier, J. (1926). *Textbook of the Practice of Medicine*, edited by F. W. Price, 2nd ed. Oxford Univ. Press, London.
Courville, C. B. (1945). *Pathology of the Central Nervous System*, 2nd ed. Pacific Press, California.
Gowers, W. R. (1893). *Diseases of the Nervous System*, 2nd ed. Churchill, London.
Griggs, D. E., and Olsen, C. W. (1937). *Arch. Neurol. Psychiat., Chicago*, 38, 564.
Jordan, W. R. (1936). *Arch. intern. Med.*, 57, 307.
Marinesco, G. (1903). *Neurol. Zbl.*, 22, 94.
Martin, M. M. (1953). *Lancet*, 1, 560.
Nonne, M. (1896). *Berl. klin. Wschr.*, 33, 207.
Pryce, T. D. (1893). *Brain*, 16, 416.
Richardson, A. T. (1952). *Ann. phys. Med.*, 1, 88.
Rudy, A., and Epstein, S. H. (1945). *J. clin. Endocr.*, 5, 92.
Rundles, R. W. (1945). *Medicine, Baltimore*, 24, 111.
Williamson, R. T. (1904). *British Medical Journal*, 1, 122.
Woltman, H. W., and Wilder, R. M. (1929). *Arch. intern. Med.*, 44, 576.

DIABETIC NEUROPATHY

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The changes which occur in the nervous system in diabetes were carefully studied in this country and in France before the end of the last century (Bouchard, 1884; Pavy, 1885; Auché, 1890). Williamson (1907, 1911, 1924) added further material. The subject was then neglected until interest was revived by the work of Jordan (1936). A considerable literature has accrued since then in the United States, but little has derived from this country.

On a routine examination of diabetic patients in hospital we found that neurological abnormalities were more the rule than the exception, and that acute nervous diseases were by no means rare. We have collected these acute cases and have also examined a consecutive series of 100 diabetic out-patients. For comparison, we studied 100 unselected chronic in-patients.

The present communication records the illnesses we encountered and attempts to analyse the significance of our findings.

Of the 100 diabetic out-patients, 57 showed neural abnormalities and three had an acute neurological illness at the time of examination. These figures agree with those of Jordan (1936), who found similar changes in 45.3% of his cases, with 2.5% suffering from "real neuritis." Rundles (1945) found neuritis in 4.5% of his cases but excluded abnormalities related to hyperglycaemia and also those which cause no symptoms. The incidence rates of diabetic neuropathy recorded in the literature vary from nil to over one-half. Such variation is explained only by the fact that the lesions discussed have often not been defined.

To reach a fuller clinical assessment of acute neuritic illness occurring in diabetes we have studied a further group of 50 patients. These were specially selected from among hospital in-patients, and therefore the findings in this group carry no indication of the incidence of the condition.

Classification and Terminology

We think that the comprehensive term "diabetic neuropathy" may be used to include all neurological changes occurring in diabetic subjects in whom there is no evidence of any alternative aetiological factor. Our cases have fallen most naturally into a scheme similar to that proposed by Grube (1899) in a neglected contribution. He wrote: "We have therefore three manifestations of nervous disturbance caused by the increase of sugar in the blood: (1) cramps or an acute irritation of the nerves; (2) neuritis or an acute inflammation of the nerves; and (3) a slow degeneration or nutritive change in the nerves."

No classification of the conditions under review has been generally accepted. The earlier schemes (Bernard

and Féré, 1882; Leyden, 1888; Williamson, 1907; Kraus, 1920) were based predominantly on symptomatology. Mauriac *et al.* (1932) distinguished true diabetic neurological changes from "paradiabetic complications" occurring in older subjects. Later classifications (Root and Rogers, 1930; Jordan, 1936; Treusch, 1945, 1947) attempted to separate degenerative and vascular features.

In a satisfactory classification the neurological findings must be related to the diabetic state of the patient. We have accepted adequate diabetic control as fulfilling the following negative criteria: the absence of thirst or polyuria, of weight loss, of ketosis, and of any but intermittent and mild glycosuria.

Based on the natural history of the conditions we have met, the following classification has been found to have practical value.

(a) Hyperglycaemic Neuropathies

These are acute conditions, coincident with hyperglycaemia and rapidly relieved by diabetic control. Pain and paraesthesiae are common, but objective signs are rare. Symptoms and signs usually clear in less than a week under routine measures, but abnormal signs sometimes persist for weeks or even indefinitely.

Hyperglycaemic neuropathies are seldom of clinical importance, being merely additional features in the presenting syndrome of lack of diabetic control. We have encountered such conditions under all circumstances of hyperglycaemia.

Case 1.—A housewife aged 63 had diabetes for ten years, moderately controlled by diet. She was admitted to hospital with pneumonia; there was heavy glycosuria without ketosis. The blood sugar was 377 mg. per 100 ml. She complained of recent pain in the right thigh, which was found to be tender. The right knee-jerk and both ankle-jerks were absent; vibration sense was absent at the ankles. The right thigh was wasted. The pneumonia was treated, and the diabetes was stabilized with insulin. Pain improved in six days and the reflexes and symptoms became normal.

Case 2.—A tailor's cutter aged 36 complained of aching of the limbs for five months and of thirst and polyuria for three months. Diabetes was confirmed. The calf muscles and Achilles tendons were abnormally tender and the tendon reflexes in the legs much reduced. Diabetic control was effected by diet and insulin, and after six days the pain and tenderness had gone and the ankle-jerks were normal. Two months later the knee-jerks had reverted to normal.

(b) Active Neuropathies

This group includes the most severe and complex of the diabetic neurological occurrences, and the patients show a wide range of signs and symptoms. An acute onset is common and there is a striking tendency to spontaneous relapse and remission unrelated to alteration in diabetic control.

Eight of our cases have shown more than one episode while under observation, and others gave a history suggestive of previous attacks. Different zones and functions of the nervous system have been involved successively. The duration of attacks has been from a few weeks to over a year. Rundles (1945) and Spear (1947) have described such recurrences, as did Jordan (1936), who noted remission of an attack after seven years. This pattern has been so striking a feature that we have suspected the condition to be fundamentally cyclic. So far, however, many cases have shown only one episode. Nearly all our cases have become symptom-free at some stage, but on the present evidence one cannot claim such a course to be invariable. In the two exceptions which we have met both patients died during an acute neurological illness. Two of our cases have developed new lesions while old ones were regressing.

Case 3.—A housewife aged 56 had diabetes for many years which was controlled by diet and insulin. One year previously she had complained of pain and weakness in the left leg, which cleared after nine months. Four months later she noticed similar symptoms in the right leg, and the knee-jerks were found to be diminished and the ankle-jerks absent. The right foot showed hyperaesthesia and the right quadriceps femoris muscle was abnormally tender. Vibration, position, and deep-pressure sense were absent in both legs. Parenteral vitamin-B_1 therapy for ten days was ineffective. The pain and weakness became disabling and persisted for a year, during which time the tendon reflexes returned in the unaffected leg. Pain then developed in the left arm, which showed evidence of an ulnar-nerve lesion. Except for a short period before the onset of the last episode, diabetic control had been good. There were no clinical vascular abnormalities and the C.S.F. was normal.

Case 4.—A retired policeman aged 74, an active and well-preserved man, had been in poor diabetic control for 16 years. One year previously he began to have pain, of intolerable intensity at night, in the left leg. The affected leg was weak, with an absent knee-jerk. He noticed drop-foot on the same side. The condition improved for six months, when the right leg became similarly affected. The thigh muscles and the dorsiflexors of the feet were found to be weak, the right more severely affected than the left. Vibration and position sense were lost in both legs. There was no abnormal muscle tenderness. The blood sugar, after 50 g. of glucose, rose to 300 mg. per 100 ml.; the C.S.F. protein was 70 mg. per 100 ml.; globulin showed slight excess.

(c) Asymptomatic Neuropathies

These are common conditions and are chronic. They present with signs alone. Recovery does not occur, and there is no clinical or pathological evidence of a progressive lesion. Of our out-patients 54% were affected in this way. The most usual findings have been reduction or absence of the tendon reflexes in the legs, together with the absence of vibration and deep-pressure sensation. Hyperaesthesia and hypalgesia often occurred asymmetrically and the pupillary responses were altered. Elderly mild diabetics most commonly show these features. Arteriosclerosis was not always present, and we have seen typical changes in young patients with recent diabetes. The main importance of this group, clinically, lies in differential diagnosis.

This working classification is not rigid. An acute neurological illness may supplant a chronic neuropathy or may be succeeded by a chronic stage. Different anatomical areas may be affected in two stages, as has been noted by Auché (1890), Rundles (1945), and Root and Crus Mascarenhas (1946).

Clinical Presentation

The evidence we have collected indicates that the diabetic neuropathies may affect any level of the nervous system. Predominantly, the peripheral nerves are involved. In a generalized disease, anatomical classification is not of value, but the relative frequency of certain syndromes calls for special mention. Some more obscure presentations will be noted. Trousseau (see Ingelrans, 1925) pointed out that "it is not rare for diabetes only to reveal itself in bizarre neurological occurrences."

1. Pain

Pain is the most important manifestation of active diabetic neuropathy. We have been able to confirm the descriptions of its characteristic nature—cramp-like, twitching, or burning, and almost invariably worse at night but uninfluenced by posture. The intensity may be extreme and the response to analgesics poor. The colour and temperature of an affected limb and the local pulses are unaltered during an attack.

Abnormal sensory signs are commonly present in association, and are the most frequent objective evidence of diabetic neuropathy. The most frequent abnormality is loss of vibration sense in the legs. Sensory change may occur in single or multiple areas, or it may be distal or limited to the area of distribution of one or more peripheral nerves. In one of our cases sensory loss was present in the zones of both ulnar nerves and one external popliteal nerve. There were paraesthesiae, and the small muscles of the hands were wasted. In six months of excellent diabetic control one arm improved, one was unchanged, and the foot lesion deteriorated.

We have seen four examples of the "painful foot" syndrome (Fein *et al.*, 1940) : severe burning pains in both feet were associated with diminished leg reflexes and sensory loss of distal distribution. One patient, a mule spinner (an occupation in which it is customary to work barefoot), had to wear slippers to alleviate the pains in his feet, but, nevertheless, preferred to tolerate the thirst of uncontrolled diabetes to the pain of walking to obtain a drink. A second case was also hyperglycaemic in type. Both responded to diabetic control, but two further cases were uninfluenced by treatment, including massive vitamin-B_1 therapy.

Three patients have been seen with clinical manifestations resembling active tabes dorsalis. A man of 45, who made a complete recovery within a year, had recent and uncontrolled diabetes. He had severe lightning pains, irregular pupils which responded poorly to light and briskly to accommodation, absent ankle-jerks, diminished knee-jerks, and absent tendon sensation at the heels. There was no other evidence of syphilis, and the C.S.F. and serological tests were normal.

2. Weakness and Wasting

The most striking component of diabetic neuropathy is weakness and wasting of the quadriceps femoris muscle. We have seen 12 examples.

Case 5.—A labourer aged 67 was admitted to hospital with a history of diabetic symptoms for one year, but his complaint was of pain in the right thigh, worse at night, of recent sudden onset. Diabetes was confirmed. Examination showed contracted pupils which responded sluggishly to light. The knee-jerks were diminished and the ankle-jerks absent. The right quadriceps femoris muscle was wasted. The C.S.F. showed a protein level of 72 mg. per 100 ml., but was otherwise normal. After three months, despite good diabetic control, symptoms and signs progressed. The C.S.F. protein was 78 mg. per 100 ml. and a myelogram was normal. Six months later he made a complete recovery and was sign-free, but had developed intermittent claudication and the pulses in his feet had been lost.

The condition may be associated with anterior crural pain and may occur in one or both legs. In one of our cases the legs were successively involved.

We have seen foot-drop in six patients. In one case the onset was bilateral ; in another case sudden onset in one foot was succeeded some months later by an insidious onset in the other. Weakness and wasting of the small muscles of the hands has been seen four times. In one patient the condition recovered with diabetic control, but the other cases were unrelated to hyperglycaemia and abnormal signs were present elsewhere.

Auché noted that muscle involvement in diabetes might resemble the Aran–Duchenne or scapulo-humeral myopathies. We observed a patient of 74 with gross wasting and weakness of the pelvic and shoulder-girdle muscles far beyond the limits of senile change. The legs and forearms were spared. The condition was static and asymptomatic.

3. Autonomic Nervous System

We have observed four patients in whom diabetic gangrene appeared to have a neuropathic basis. In all, the gangrene was painless and recovered completely. In none were the peripheral pulses, colour, or temperature at the extremities abnormal, and all showed other evidence of neuropathy. In one case the condition relapsed three times, but amputation was averted by spontaneous healing with coincident improvement in the neurological state. One year later the foot remained in good condition.

The suggestion that certain cases of painless gangrene have a neuropathic rather than a vascular basis has practical importance. In the presence of clinically normal peripheral vessels and evident neuropathy, a prolonged trial of conservative management may avert amputation. Such a view is supported by the reports of Holt (1928), McKittrick and Root (1928), Bailey and Root (1942), de Takats (1945), and Joslin (1946).

We have seen one case of Charcot joint affecting the mid-tarsal region. Perforating ulcer and Charcot joints have been described by Pryce (1887), Auché (1890), Bramwell (1907), Williamson (1911), de Takats (1945), Bailey and Root (1947), Morris (1947), Shore (1947), and Foster and Bassett (1947).

Painless distension of the bladder with retention and sometimes urinary infection were seen in four cases, and resembled the reports of Jordan and Crabtree (1935), Gill (1936), and Rudy and Muellner (1941).

A typical example of diabetic nocturnal diarrhoea has been studied. This resembled the cases of Sheridan and Bailey (1946). The apparently specific effect of liver injections is hard to interpret, but they make the recognition of the syndrome important. One of us referred to the use of vitamin B_{12} in this condition (Hirson, 1951).

Case 6.—A housewife aged 63 had poorly controlled diabetes for eleven years and usually suffered paraesthesiae and pains in the legs. For seven years she had intermittent diarrhoea, worse at night, with faecal incontinence of "dirty brown water—like mud." Some attacks persisted for weeks. On examination there was marked retinopathy, and the ankle-jerks and vibration sense in the legs were absent. Gastro-intestinal investigations, including laparotomy, were negative, but the administration of crude liver extract by injection led to a complete remission, which, when she was last seen, had lasted for over a year. Previous remissions seldom exceeded two weeks. Diabetic control remained poor.

A fundamental study of the abnormalities of the autonomic nervous system in diabetes was made by Rundles (1945), who found postural hypotension, and visceral, vascular, and temperature-regulator abnormalities.

4. Cranial Nerves

We have seen a complete third-nerve lesion which we considered to be due to diabetes and which recovered completely and spontaneously (see Case 8 below). Similar lesions have been reported by Cerise and Bollack (1913), Ingelrans (1925), Root (1933), and Herson (1948). Most of the cranial nerves have been reported to be involved in diabetic neuropathies, usually as an active occurrence. We have twice seen Argyll Robertson pupils, also noted by Jordan (1936), Herman (1939), and Smith (1949).

5. Other Manifestations

While the conditions which we have so far described have clinically involved the peripheral nervous system, in a single case the central nervous system was also involved. The presentation resembled that of a subacute combined degeneration of the cord with peripheral nerve change, and later development suggested an encephalitis.

Case 7.—A housewife aged 65 had diabetes for two years, satisfactorily controlled by diet and insulin. She developed stiffness and weakness of the legs, with ataxia and paraesthesiae of the extremities. She was bedridden, and on admission to hospital showed a heavy glycosuria without ketosis. Both legs were spastic, the tendon reflexes were exaggerated, and clonus was present. Both plantar responses were extensor. There was widespread peripheral sensory loss. The blood and sternal marrow were normal. Despite stringent diabetic control and massive vitamin-B_1 therapy, the condition progressed. Trophic ulcers of the feet and sphincter incontinence developed, and there was mental confusion. She died unrelieved. Full neuro-pathological examination by Dr. E. Pollack revealed no specific lesions. There was considerable arteriosclerosis.

Griggs and Olsen (1937) and Rudy and Epstein (1945) reported similar cases.

Panatrophy (Kinnier Wilson) has been noted in four cases. This condition has not been fully described in diabetes before. Localized areas of profound wasting of muscle and subcutaneous tissues were found at sites far removed from possible insulin injections.

Although polyneuritis is commonly mentioned as a neurological complication of diabetes, we have not seen any example of the classical sensorimotor symmetrical polyneuritis running a typical course (Walshe, 1946). Further, we have found in the literature only a single case (Pitres and Marchand, 1917) which satisfied the usual diagnostic criteria.

The Cerebrospinal Fluid

The cerebrospinal fluid was examined 19 times in 18 of our patients. In six cases the protein level was above 50 mg. per 100 ml., the highest figure being 78 mg. per 100 ml. (in Case 5). Four months previously the same patient had shown a level of 72 mg. per 100 ml. Five of the six patients had severe active neuropathies, but one showed only mild change. Four patients (aged 40, 55, 63, and 70 years) had protein levels between 40 and 50 mg. per 100 ml. In all, the cell count and Wassermann reaction were normal.

These findings are in accord with those of Jordan (1936), Joslin and Root (1939), and Rundles (1945). We have not found the extreme levels up to 390 mg. per 100 ml. of protein previously recorded. There has been no direct correlation between the protein level and the degree of neurological change; although the highest levels have been found in severe neuropathies, some severe cases have shown normal levels. In the asymptomatic group the findings have been normal.

Aetiology

Two main causal factors have been proposed by previous workers—arteriosclerosis and vitamin-B deficiency. Arteriosclerosis shows a high incidence in diabetes, and Dolger (1947) regarded such change as "an associated concomitant" of the disease. The cyclic nature of some of our cases makes it seem unlikely that the lesions we describe are due to irreversible vascular change. We have seen neuropathies of all types in patients under the age of 30 and in older patients with clinically normal vasculature. By contrast, some severely arteriosclerotic diabetics have shown no nerve change.

To compare the neurological signs of diabetes with those of arteriosclerosis 100 elderly in-patients were examined. All were in the chronic wards of a former municipal hospital, and the only cases excluded from a consecutive series were those under the age of 50, those whose mental state prevented adequate examination, and those with fixed joints. We examined, in particular, the tendon reflexes, pupils, vibration sense, and tendon-pressure sensation. There was no significant difference in the findings in those patients with and those without normal palpable pulses at the ankles. Inevitably, in view of the multiple conditions present, no evidence of a consistent neurological picture emerged, but there was no overall similarity to that of our diabetic cases (Table I). Woltman (1929) and Critchley (1931) also commented on the varied findings in arteriosclerosis.

TABLE I.—*Comparison of Abnormal Findings*

	100 Consecutive Diabetic Out-patients (Av. Age 54·3 Years)	100 Consecutive Chronic In-patients (Av. Age 73 Years)
Knee-jerks absent	19	22
,, diminished	31	9
,, exaggerated	6	74
Ankle-jerks absent	63	42
,, diminished	16	19
,, exaggerated	0	37
Vibration sense absent at knee	27	71
,, ,, ,, ,, ankle	50	89
Achilles tenderness increased	4	39
,, ,, decreased	32	8

Notes: (1) The findings in both legs are reported. (2) All patients in these two series were jointly examined by the same observers. (3) Of the chronic in-patients 13 showed significant pupillary change. Allowing for detectable disease (cerebral lesions, tabes, etc.), 12 patients showed unexplained reduction or absence of knee-jerks and 15 unexplained reduction or absence of ankle-jerks. The corresponding figures for increase of the reflexes was 20 and 14. In the only two diabetic patients in this group the diagnosis was suggested on the basis of the neurological findings only.

The pathological studies of Woltman and Wilder (1929), which have provided the main experimental evidence for a vascular aetiology, were conducted on limbs amputated for gangrene. This selection seems to invalidate their conclusions, but, even within this selected group, the authors notice that "there is not an accurate correlation between the degree of degeneration and the neurological symptoms." We have been impressed by the disparity between the consistent picture of the chronic diabetic neuropathies and the diverse findings in arteriosclerosis. Taken in conjunction with the considerations outlined above, we think it unlikely that diabetic arteriosclerosis causes neuropathy.

The therapeutic value of vitamin-B_1 administration (Vorhaus, 1939; Aring *et al.*, 1939; Fein *et al.*, 1940) has been the basis of the deficiency theory of the diabetic neuropathies. We have been unable to reproduce such results in active or chronic cases, and have had no need to conduct a therapeutic trial in hyperglycaemic cases. We have found, in our patients, no other evidence of vitamin deficiency, which would be anticipated if the hypothesis were correct. Rowlands and Wilkinson (1938), Sinclair (1938), Needles (1939), and Pollack *et al.* (1941), found no biochemical evidence of vitamin-B_1 lack in their cases. Lowry and Hegsted (1945) found that rats rendered diabetic with alloxan had reduced vitamin-B_1 requirements.

The claim that a chronic vitamin deficiency can respond rapidly to specific treatment is in itself surprising, as late beriberi, for example, does not respond in this way. In acute lesions a response might be expected, but such has not been our experience, and, by contrast, spontaneous remissions often occur.

We have found that neither the sex of the patient nor the type or severity of diabetes is related to neuropathy. Table II analyses the findings in our out-patient group. In general, the asymptomatic cases occur in the older age groups and the more severe active cases are commonest in middle life.

TABLE II.—*Neurological Findings in 100 Unselected Diabetic Out-patients*

	No. of Subjects	No. with Neurological Abnormalities
Total cases	100 (av. age 54·3 years)	57 (57%)
Males	23 (,, ,, 46·4 ,,)	13 (56·5%)
Females	77 (,, ,, 58·1 ,,)	44 (57·1%)
Under 30 years	8	3
30–50 ,,	22 } 30	9 } 12 (40%)
50–70 ,,	61	38
Over 70 ,,	9 } 70	7 } 45 (64·3%)
Diabetes less than 1 year	15	7
,, 1–3 years	23 } 63	14 } 37 (58·7%)
,, 3–5 ,,	25	16
,, 5–10 ,,	18	9
,, over 10 years	19 } 37	11 } 20 (54·0%)
Controlled on insulin	68	39
,, without insulin	14 } 82	10 } 49 (59·7%)
Uncontrolled on insulin	6	4
,, without insulin	12 } 18	4 } 8 (44·4%)

The role of hyperglycaemia in the causation can be interpreted only in relation to the classification groups. Most of the patients presenting with uncontrolled diabetes and neurological abnormalities respond rapidly to routine treatment. These form our first group. The rest, together with patients who are in good control and yet show nerve change, fall into our second and third groups. The significance of previous episodes of hyperglycaemia or ketosis cannot be assessed, since such states are almost universal, at least at the onset of diabetes. We will refer to cases in which neuropathy preceded clinical diabetes (Cases 8 and 9). Bonkalo (1950) finds that his experience "tallies well with the generally acknowledged fact that there is no direct connexion between blood sugar and neuritis."

In hyperglycaemic neuropathies the sole factor has been the failure of diabetic control. Neurological features occur only in a proportion of diabetics who are out of control, and no predisposing factors have been found in such cases. However, the frequency of pain in diabetic ketosis is well known.

Treatment

Symptomatic treatment, including heavy sedation, and physiotherapy are needed in most active cases. Optimum diabetic control will be indicated on general grounds, but this produced striking results only in our first group. It is justifiable, however, to observe the effects of insulin on any acute case even when control is apparently adequate on diet alone.

De Takats (1945) claimed that lumbar sympathectomy gave relief from leg pains. Sandstead and Beams (1938) advocated large dosage of sodium chloride, but we have had no success with a small group of cases treated by this method. Vitamin B_{12} was not available at the time of these investigations.

Wagener (1945) noted, in respect to diabetic retinopathy, that present methods of diabetic control are unsatisfactory. We hold this to be equally true of diabetic neuropathy.

Discussion

There is no good evidence that the incidence of neurological change in diabetes is materially less than in the "pre-insulin" era. The onset of neuropathy may have been delayed in the diabetic life.

We have described and emphasized the more common presentations, but the obscurity of some manifestations is noteworthy. Root (1933), Jordan (1936), and Wilder (1940) have listed alternative diagnoses which have needed consideration. Our experience also has been of the need to exclude a wide range of neurological conditions and even of intrathoracic and abdominal diseases.

In two cases neuropathy presented in subjects in whom neither clinical evidence of diabetes was found at the time nor any alternative cause for their condition. In Case 8, one year after the first neurological illness, clinical diabetes developed with a second episode of neuropathy, and in Case 9 the type of pain, in association with the glucose-tolerance curve, indicated the true diagnosis.

Case 8.—A housewife aged 65 presented with a complaint of pain around the left eye and developed left-sided ptosis and external ophthalmoplegia. The C.S.F. showed a protein level of 45 mg. per 100 ml. and was otherwise normal. An *x*-ray film of the skull and the Wassermann reaction were negative. There were no constitutional symptoms and no glycosuria. Angiography was not undertaken, as rapid spontaneous remission occurred. One year later she complained of pain, worse at night, in the right breast and the thigh. The Achilles tendon sensation was exaggerated and vibration sense was lost in the legs. She had glycosuria and mild diabetic symptoms. The blood sugar rose to 278 mg. per 100 ml. The diabetes was controlled by diet alone. After three months she was sign- and symptom-free.

Case 9.—A housewife aged 55 attended hospital complaining of the symptoms of right ulnar neuritis. Sensation was impaired in the area of distribution of that nerve and examination was otherwise normal. Spurling's sign was negative. Gross radiological osteoarthritis of the cervical spine, suggesting a neurogenic arthropathy, was present. The description of the pain was typical of diabetic neuropathy. Pain was unrelieved despite prolonged immobilization of the neck in a plaster collar. Only one of a series of urine tests showed sugar to be present, but the glucose-tolerance curve, after 50 g. of glucose, gave half-hourly blood-sugar levels of 98, 172, 212, 188, and 141 mg. per 100 ml. Spontaneous remission of the pain occurred after four months.

Claude (1911) thought that neurological change might precede diabetes, and Jordan (1943) reported seven cases of neuropathy in patients without clinical diabetes who had abnormal glucose-tolerance curves.

Thus, even in the absence of glycosuria or constitutional symptoms we believe that the blood-sugar curve may be of value in the diagnosis of obscure neurological problems.

Our findings have a bearing on the fundamental considerations of diabetic pathology. They offer support to the view that diabetes is a disease-complex in which the metabolic disorder is only one manifestation, with neuropathy occurring not as a "complication" but as an integral part of a variable process. Dry and Hines (1941) presented similar views with regard to arteriosclerosis in diabetes, writing that "an inherent weakness or abiotrophy exists which affects both the insulin-producing tissues and the vascular system which require, in each instance, only an additional stimulus to bring about pathologic change." Wagener (1945), studying retinopathy, added similar evidence, and Gilbert and Dunlop (1949) showed a variation from normal in the obstetrical history of females who later developed diabetes.

Jordan and Randall (1936) and Jordan, Randall, and Bloor (1935) described changes in the lipoid content of nervous tissue from patients with diabetic neuropathy which was not present in control material from arteriosclerotic subjects. Sirek *et al.* (1950) record abnormal levels of blood phospholipids in their cases. These findings require further study.

Conclusions

About half of all cases of diabetes mellitus show evidence of neurological disease.

Diabetic neuropathy may be divided into three groups: (*a*) hyperglycaemic—related to failure of control and rapidly relieved by routine treatment; (*b*) active—the most serious form, present in about 3% of all cases, unrelated to diabetic status and with a tendency to remission and relapse; and (*c*) asymptomatic—chronic, permanent, and not disabling.

There is no good evidence that arteriosclerosis or vitamin-B_1 deficiency is a causal agent. The neuropathic process seems to be inherent in some cases of diabetes.

The glucose-tolerance curve is of value in the investigation of obscure neurological disease.

The production of gangrene, neurogenic bladder, and joint change by diabetic neuropathy is of practical importance.

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REFERENCES

Aring, C. D., Evans, J. P., and Spies, T. D. (1939). *J. Amer. med. Ass.*, **113**, 2105.
Auché, B. (1890). *Arch. Méd. exp.*, **2**, 635.
Bailey, C. C., and Root, H. F. (1942). *J. clin. Invest.*, **21**, 649.
—— —— (1947). *New Engl. J. Med.*, **236**, 397.
Bernard, D., and Féré, C. (1882). *Arch. Neurol., Paris*, **4**, 336.
Bonkalo, A. (1950). *Arch. intern. Med.*, **85**, 944.
Bouchard, C. (1884). *Progr. méd., Paris*, **12**, 819.
Bramwell, B. (1907). *Clin. Stud.*, **5**, 279.
Cerise, L., and Bollack, J. (1913). *Rev. neurol., Paris*, **26**, 115.
Claude (1911). *Med. Press*, **143**, 140.
Critchley, M. (1931). *Lancet*, **1**, 1119, 1221, 1331.
de Takats, G. (1945). *Proc. Amer. Diabetes Ass.*, **5**, 183.
Dolger, H. (1947). *J. Amer. med. Ass.*, **134**, 1289.
Dry, T. J., and Hines, E. A., Jun. (1941). *Ann. intern. Med.*, **14**, 1893.
Fein, H. D., Ralli, E. P., and Jolliffe, N. (1940). *J. Amer. med. Ass.*, **115**, 1973.
Foster, D. B., and Bassett, R. C. (1947). *Arch. Neurol. Psychiat., Chicago*, **57**, 173.
Gilbert, J. A. L., and Dunlop, D. M. (1949). *British Medical Journal*, **1**, 48.
Gill, R. D. (1936). *J. Urol.*, **36**, 730.
Griggs, D. E., and Olsen, C. W. (1937). *Arch. Neurol. Psychiat., Chicago*, **38**, 564.
Grube, K. (1899). *Lancet*, **2**, 203.
Herman, M. (1939). *Arch. Neurol. Psychiat., Chicago*, **41**, 800.
Herson, R. N. (1948). *Proc. roy. Soc. Med.*, **41**, 104.
Hirson, C. (1951). *Lancet*, **2**, 1227.
Holt, E. (1928). *J. Amer. med. Ass.*, **91**, 959.
Ingelrans, L. (1925). *Médecine*, **7**, 381.
Jordan, W. R. (1936). *Arch. intern. Med.*, **57**, 307.
—— (1943). *Sth. med. J.*, **36**, 45.
—— and Crabtree, H. H. (1935). *Arch. intern. Med.*, **55**, 17.
—— and Randall, L. O. (1936). Ibid., **57**, 414.
—— —— and Bloor, W. R. (1935). Ibid., **55**, 26.
Joslin, E. P. (1946). *The Treatment of Diabetes Mellitus*, 8th ed. Kimpton, London.
—— and Root, H. F. (1939). *Trans. Ass. Amer. Phys.*, **54**, 251.
Kraus, W. M. (1920). *Med. Clin. N. Amer.*, **4**, 225.

Leyden, E. (1888). Cited by Ross and Bury (1893).
Lowry, P. T., and Hegsted, D. M. (1945). *J. Lab. clin. Med.*, **30**, 839.
McKittrick, L. S., and Root, H. F. (1928). *Diabetic Surgery*. Lee and Febiger, Philadelphia.
Mauriac, P., Broustet, P., and Traissac, E. J. (1932). *Paris. méd.*, **2**, 19.
Morris, M. H. (1947). *N.Y. St. J. Med.*, **47**, 1395.
Needles, W. (1939). *Arch. Neurol. Psychiat., Chicago*, **41**, 1222.
Pavy, F. W. (1885). *Lancet*, **2**, 1033.
Pitres, A., and Marchand, L. (1917). *Progr. méd., Paris*, **36**, 295.
Pollack, H., Ellenberg, M., and Dolger, H. (1941). *Arch. intern. Med.*, **67**, 793.
Pryce, T. D. (1887). *Lancet*, **2**, 11.
Root, H. F. (1922). *Med. Clin. N. Amer.*, **5**, 1433.
—— (1933). Ibid., **16**, 985.
—— and Crus Mascarenhas, C. (1946). *Amer. J. dig. Dis.*, **13**, 173.
—— and Rogers, M. H. (1930). *N. Engl. J. Med.*, **202**, 1049.
Ross, J., and Bury, J. S. (1893). *On Peripheral Neuritis*. Griffin, London.
Rowlands, E. N., and Wilkinson, J. F. (1938). *British Medical Journal*, **2**, 878.
Rudy, A., and Epstein, S. H. (1945). *J. clin. Endocr.*, **5**, 92.
—— and Muellner, S. R. (1941). *J. Urol.*, **45**, 844.
Rundles, R. W. (1945). *Medicine*, **24**, 111.
Sandstead, H. R., and Beams, A. J. (1938). *Arch. intern. Med.*, **61**, 371.
Sheridan, E. P., and Bailey, C. C. (1946). *J. Amer. med. Ass.*, **130**, 632.
Shore, T. H. G. (1947). *Lancet*, **2**, 738.
Sinclair, H. M. (1938). *Proc. roy. Soc. Med.*, **32**, 812.
Sirek, O. V., Bonkalo, A., and Möllerström, J. (1950). *Arch. intern. Med.*, **85**, 966.
Smith, M. D. (1949). *Glasg. med. J.*, **30**, 181.
Spear, G. E. (1947). *Lancet*, **2**, 963.
Treusch, J. V. (1945). *Proc. Mayo Clin.*, **20**, 293.
—— (1947). *Ann. West. Med. Surg.*, **1**, 67.
Vorhaus, M. G. (1939). *Amer. J. med. Sci.*, **198**, 837.
Wagener, H. P. (1945). *Proc. Amer. Diabetes Ass.*, **5**, 203.
Walshe, F. M. R. (1946). *Practitioner*, **156**, 19.
Wilder, R. M. (1940). *Clinical Diabetes Mellitus and Hyperinsulinism*. Saunders, Philadelphia.
Williamson, R. T. (1907). *Rev. Neurol. Psychiat.*, **5**, 550.
—— (1911). *Diseases of the Spinal Cord*. Oxford Univ. Press, London.
—— (1924). *Practitioner*, **112**, 85.
Woltman, H. W. (1929). *J. Amer. med. Ass.*, **93**, 670.
—— and Wilder, R. M. (1929). *Arch. intern. Med.*, **44**, 576.

PROGNOSIS IN DIABETIC PREGNANCY

BY

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The observations in this communication are based on two series of diabetic pregnancies: (1) 275 pregnancies supervised and delivered at King's College Hospital, referred to as the K.C.H. series; and (2) 458 pregnancies, details of which were collected from different centres in Great Britain, and referred to as the Q series. A detailed analysis of some of this clinical material has already been published (Peel and Oakley, 1949).

I will first deal briefly with the maternal aspect and then pass on to the more controversial and less satisfactory problem of the fate of the foetus.

The Maternal Aspect

In the Q series of 458 pregnancies 13 mothers died—in eight the cause of death was diabetic coma, and three of these died undelivered. Of the remaining five deaths two were due to peritonitis and one each to pneumonia, pulmonary embolism, and eclampsia, giving a maternal mortality rate of 2.8%. In the K.C.H. series of 275 pregnancies there were four deaths due to pulmonary embolism, septicaemia, cholaemia, and massive collapse of the lung; there were no deaths in diabetic coma and none of the patients died undelivered—giving a mortality rate of 1.4%. These figures show that death attributable to diabetes still does occur, but it can always be prevented by proper supervision of the mother.

In this connexion the insulin requirement in at least 75% of cases rises during the second and third trimesters, and—what is perhaps more important—the renal threshold in about the same percentage falls at about the fourth or fifth month of pregnancy. This constitutes one of the chief difficulties from the point of view of control of the maternal diabetes, and is usually first recognized by the development of heavy glycosuria and often severe ketosis in a previously well-balanced diabetic. To overcome this it is advisable to raise the carbohydrate content of the diet to 200 g. and give the mother a morning injection of soluble insulin and a second injection before tea of soluble insulin mixed with enough P.Z.I. to render the morning urine free of acetone bodies. If ketosis persists the addition of about 20 g. of glucose to each of the four meals usually clears it up. It is now well known that the maternal mortality rate can in this way be kept to a very low figure, but less is known about maternal morbidity of diabetics following pregnancy. The following points were therefore investigated: (1) insulin requirement following pregnancy; and (2) incidence and aggravation of diabetic complications: (*a*) retinitis, (*b*) hypertension, and (*c*) albuminuria. In none of the last 80 pregnancies of the K.C.H. series was there any significant increase in insulin requirement following pregnancy and attributable to it.

As regards retinitis, four cases were of interest—two were patients of Dr. Lawrence's and two of mine. Both of Dr. Lawrence's cases developed severe retinal haemorrhages, mostly of the flame or linear variety, and in one case these were associated with oedema of the optic disks; in both, the retinal lesions disappeared after the pregnancy. In my cases—both long-standing diabetics of 21 and 13 years' duration—there were previous ocular complications; in the former severe bilateral diabetic cataracts which made it difficult to exclude the presence of early retinitis, and in the latter typical early retinitis. During pregnancy the former developed definite aneurysms, blob haemorrhages, and patches of early exudate, and these have since progressed to retinitis proliferans with severe loss of vision. In the other case the retinitis has progressed since pregnancy. In both cases there has been an increase in albuminuria and a rise in blood pressure. These two cases are mentioned in detail because, from the maternal point of view, they are of great importance in connexion with the decision whether or not, in long-standing diabetics, pregnancy should be advised or be allowed to proceed. In the remaining 10 cases with retinitis at the onset of pregnancy there has been no appreciable change or evidence of deterioration, although two of them have been through two pregnancies. It is possible, therefore, that the progression of the retinal complication in the two cases would have occurred quite apart from the pregnancy, as, in fact, it very often does in such long-standing cases.

The question of hypertension and albuminuria is considered in connexion with toxaemia of pregnancy.

Toxaemia of Pregnancy

It is generally recognized that toxaemia is a relatively frequent complication of diabetic pregnancy. It is referred to again in connexion with foetal mortality, but I thought it would be worth while trying to follow up the toxaemic cases with a view to finding out whether they showed an unexpectedly high incidence or rapid development of hypertension and albuminuria following pregnancy. Interpretation of results is made difficult by the small number of cases and the fact that diabetics are apt to develop hypertension and albuminuria quite apart from pregnancy; some help, however, is to be gained from the relatively young age of the patients studied and the recognized association between these complications and the duration of the diabetes.

Of the last 222 diabetic pregnancies at King's College Hospital, 24 have been complicated by toxaemia, which on two occasions has occurred with successive pregnancies in the same patient. Three of the 24 cases are untraced, one died with eclamptic fits and cholaemia a few hours after delivery of a normal child which survived, and one had uraemia due to chronic nephritis. The remaining 19 cases have been followed with special reference to hypertension, albuminuria, and retinitis. In 13 there is no evidence of change in any of these respects following the toxaemic pregnancy, the only instance of hypertension being in a woman who had a benign essential hypertension before the pregnancy,

TABLE I.—*Late Effects of Toxaemia of Pregnancy*

Case No.	Before Toxaemia				After Toxaemia			
	B.P.	Alb.	Retinitis	Interval	B.P.	Alb.	Retinitis	Duration of M.D.
1	Normal	0	0	4 yrs.	132/98	0	0	12 yrs.
2	130/90	Sl. trace	?	7 ,,	120/90	0	Severe	11 ,,
3	148/80	0	0	4 ,,	170/90	0	0	11 ,,
4	130/80	Trace	0	1½ ,,	160/90	Sl. trace	0	23 ,,
*5	130/90	,,	0	¾ yr.	130/80	++	Early mild	16 ,,
*6	130/80	0	0	4 yrs.	160/100	0	0	10 ,,
				8 ,,	195/110	0	0	14 ,,

* Two toxaemic pregnancies.

which was no worse after it. The remaining six cases are summarized in Table I. It will be noted that both patients who had two toxaemic pregnancies are included in this small series. It is also interesting that in all six cases the diabetes had been present for 10 or more years; but this makes the interpretation of results more difficult, as diabetes of this duration may, quite apart from pregnancy, be associated with some hypertension, albuminuria, and retinitis. In these circumstances, it would be quite wrong to conclude that toxaemia of pregnancy constitutes a graver danger to the diabetic than to the non-diabetic mother, and I think the same can probably be said regarding the child.

Fate of the Foetus

Let me now turn to the prognosis in diabetic pregnancy from the point of view of the child. That an abnormally high percentage of these pregnancies result in stillbirth or neonatal death cannot be denied, that many different theories have been put forward to account for this high foetal loss also cannot be denied, but the fact that we still know little or nothing of the cause of this loss, if not actually denied, is being obscured, in my opinion, by the unwarranted acceptance of unproved theories and uncontrolled experiments. The results of the two series of pregnancies—733 cases in all—are applied to some of the theories put forward to account for this high foetal mortality rate in order to show that none of these theories will stand up to a critical analysis of a sufficiently large series of diabetic pregnancies.

(1) Control of the Maternal Diabetes

In 1942 Lawrence and Oakley recorded 54 diabetic pregnancies and showed that, if these were divided into three groups according to the degree of control of the maternal diabetes, the foetal mortality rate in the worst group was

TABLE II.—*Relation of Foetal Mortality to Age of Onset of Maternal Diabetes*

Age of Onset of Diabetes	No. of Babies	Foetal Mortality
1–15	70	21 (30%)
16–24	105	24 (23%)
25 and over	92	29 (31%)

70% and in the best 23%, the intermediate group being 50%. These results suggest that poor control will raise the foetal loss rate, but also that good control will not lower it below the high figure of 23%.

(2) Severity of Maternal Diabetes

Gilbert and Dunlop (1949) have shown that there is no significant difference between the foetal mortality rate in non-insulin-treated and insulin-treated diabetic mothers; this finding has been confirmed by other workers and by me.

(3) Age of Onset of Maternal Diabetes

The relationship between the age of onset of the maternal diabetes and the foetal mortality from maceration, stillbirth, and neonatal death has been studied by Forgen Pederson (1949). In a series of 147 babies he found that when the onset of maternal diabetes was during the ages of 1 and 15 the foetal mortality rate was 42%, during 16 and 24 years 29%, and over 25 years 6%. He therefore concluded that when diabetes begins in childhood the foetal mortality rate is high; when the patient is grown-up before the onset of her diabetes the foetal mortality is far less. In order to test the validity of this statement the mortality rate in a series of 267 babies delivered of diabetic mothers at King's College Hospital was related to the age on onset of the maternal diabetes (Table II); the results obtained fail to confirm the existence of any direct relationship.

(4) Duration of Maternal Diabetes

It has also been suggested that the duration of the maternal diabetes may be a factor in the production of the high foetal mortality rate. A series of 665 pregnancies was therefore analysed from this point of view (Table III). These

TABLE III.—*Relation of Foetal Mortality to Duration of Maternal Diabetes*

Duration	Q Series				K.C.H. Series			
	Cases	S.	N.	Total	Cases	S.	N.	Total
0–4 yrs.	209	66	18	84 (40·2%)	97	19	10	29 (30%)
5–9 ,,	109	35	10	45 (41%)	72	9	11	20 (28%)
10–14 ,,	60	15	9	24 (40%)	55	4	10	14 (25%)
15–19 ,,	19	9	1	10 (52·6%)	28	4	2	6 (21%)
20+ ,,	5	2	0	2 (40%)	11	0	3	3 (27%)
Total	402	127	38	165 (41%)	263	36	36	72 (27%)

S. = Stillbirths. N. = Neonatal deaths.

figures show: the high foetal loss rate for all durations, the absence of any relationship between duration and foetal mortality, and the significantly lower mortality in the K.C.H. series, to which reference is made later.

(5) Diabetic Complications

As foetal loss could not be accounted for in terms of control, severity, or duration, it was decided to see whether the presence of retinitis or albuminuria in the mother before the onset of pregnancy could be a causal factor. Hypertension was not seriously considered, as it is almost always an indication for advising against pregnancy or, alternatively, for termination.

In spite of the relatively large number of pregnancies, these complications were found in comparatively few; 12 mothers had retinitis at the time of conception. In these 12 cases 14 pregnancies resulted in 12 live children and 2 neonatal deaths, a loss comparable to the uncomplicated pregnancies. Albuminuria, especially when associated with hypertension, is so well recognized as being associated with high foetal loss rate, even in non-diabetics, that it is not surprising that only six patients had persistent appreciable albuminuria at the time of conception and were allowed to continue; all six cases gave birth to live babies, and all survived and did well.

(6) Complications of Toxaemia of Pregnancy

Much stress has been laid on the frequency of toxaemia in these cases and upon the danger of this condition to the child. Table IV shows the results of toxaemic pregnancies in the K.C.H. and Q series. It will be seen that the toxaemic cases had a slightly higher foetal mortality rate

TABLE IV.—*Relation of Foetal Loss to Toxaemia of Pregnancy*

	Cases	Toxaemia					Total Foetal Loss
		No.	%	Live	Dead	Foetal Loss	
Q series	455	86	19·0	48	38	44·2%	40·3%
K.C.H.	274	31	11·3	21	10	32·2%	26·7%

than the others; but toxaemia is clearly not the answer, nor can one expect that any form of therapy directed against it will appreciably lower the foetal death rate.

Smith and Smith (1938) put forward the view that toxaemia of pregnancy is related to a disturbance of hormone balance and, pursuing the same line of thought, Priscilla White (1947) claims to have greatly lowered the foetal mortality rate by giving stilboestrol in increasing doses together with a daily injection of progesterone. In order to test the validity of this claim the Medical Research Council in England has organized an investigation in which a series of pregnant diabetics—selected at random—have received hormone therapy from an early stage of pregnancy, the controls being given inert tablets of identical appearance. The only ways in which treatment differed from that advocated by Priscilla White were that progesterone has been given by mouth in the form of ethisterone—daily injections being impracticable in the conditions existing in England—and the patients have not been admitted to hospital as a routine measure at least two weeks before delivery. Neither the physicians nor the obstetricians in charge know which cases have received active and which inert therapy, and it is hoped that, in this way, results of statistical significance will be obtained. Unfortunately, the results of this investigation are not yet available, but in a series of 50 pregnancies in which hormone therapy was given at King's College Hospital, 21 resulted in stillbirth or neonatal death, giving a foetal mortality of 42%.

(7) Mode and Time of Delivery

It has been shown in Table III that the foetal loss rate in the K.C.H. series was very significantly lower than that in the Q series; there are several possible causes for this. Where large numbers of cases are treated greater experience is apt to produce better results; close co-operation between diabetic and obstetric departments is also of great importance, as is regular diabetic and antenatal supervision. The main cause of the difference, however, is to be found in the time and mode of delivery.

TABLE V.—*Relation of Foetal Loss to Mode of Delivery*

Mode of Delivery	Q Series					K.C.H. Series				
	Cases	Live	S.	N.	% Loss	Cases	Live	S.	N.	% Loss
Spontaneous labour ..	129	83	23	23	35·6	17	14	2	1	18·0
Induced labour	126	91	23	12	27·8	36	23	9	4	36·0
Caesarean section ..	115	97	3	15	15·7	156	127	1	28	18·5
Total ..	370	271	49	50	27	209	164	12	33	21·5

S. = Stillbirths. N. = Neonatal deaths.

Table V shows the high loss rate associated with spontaneous labour in the Q series, the much lower figure in the K.C.H. series being due to the fact that all the cases so delivered went into labour spontaneously at or before the thirty-sixth week, at which time they would otherwise have been induced or had caesarean section. The figures for induction are high but comparable—primiparae giving a higher foetal death rate than multiparae, as might be expected. The figures for caesarean section are much lower, and again are comparable. It would appear, therefore, that in the Q series the large number of pregnancies allowed to continue to spontaneous labour accounted for the higher foetal mortality, and incidentally also for the fact that three mothers died undelivered. It will be seen from Table V that the practice in the K.C.H. series of terminating the pregnancy at about the thirty-sixth week by caesarean section or, in the case of those who have had a previous normal delivery, by induction has resulted in a great reduction in stillbirths but a considerable neonatal mortality. Until some reliable method of preventing death *in utero* in the last few weeks of pregnancy has been discovered—and I am not convinced that such a method yet exists—I feel that we are most likely to reduce the loss rate by obtaining a live baby and directing our efforts to prevent it from dying. This brings me to my last consideration—namely, the newborn baby.

The Newborn Baby.—The majority of neonatal deaths occur within 48 hours of delivery and are due to what appears to be respiratory failure; the baby has recurrent attacks of apnoea with cyanosis, in one of which it dies. Other possible causes of death are foetal hypoglycaemia and congenital deformities. The latter are relatively common, and 19 instances were observed in 221 consecutive diabetic pregnancies at King's College Hospital, giving an incidence of 8.6%. Such deformities could not be related to duration or control of maternal diabetes, and, although all the mothers were receiving insulin, there was no evidence that hypoglycaemia was more frequent or more severe than in those pregnancies which resulted in normal children.

(8) Foetal Hypoglycaemia

Although once regarded as a likely cause of neonatal death, there has recently been a tendency to discount this possibility. In order to arrive at a more definite conclusion it was decided to estimate blood sugars at two-hourly intervals on a series of babies, half of whom received no glucose and the other half 50% glucose hourly by mouth. In all, 17 babies received glucose and 18 no glucose, the respective neonatal deaths being two in the former and four in the latter series. The number of cases is too small to allow of any definite conclusions, but certain findings are of interest. In one of those that received glucose and died there was no demonstrable sugar in the blood one hour before death, while in the other the blood sugar at the time of death was 175 mg. per 100 ml. In the same series eight of those that lived had blood sugars of 30 mg. or less in the first six hours, and in four of these the level fell to 20 mg. or less; one survivor had no demonstrable blood sugar at two hours after delivery. Of the 18 babies that received no glucose, three of the four that died showed levels of 35 mg. or less per 100 ml. within six hours of death, and the remaining one had a blood sugar of 78 mg. four hours before it died. The blood sugars of six of those that lived fell below 35 mg. per 100 ml., and in four of these it was less than 20 mg. It is difficult, therefore, to say more than that death may occur with a normal blood sugar and survival with a very low one or even without any demonstrable sugar in the blood. This problem clearly needs further study.

Conclusion

Great emphasis must be laid on the importance of the nursing and management of the newborn infant. The use of an isolette in which both oxygen content of the air and temperature can be controlled, and regular suction if there are any signs of respiratory embarrassment, may help to reduce neonatal mortality. The use of continuous low-pressure suction and some form of mechanical respirator are under consideration in our department, and electrolyte and hormone studies are being carried out on these babies in the hope that they may shed some light on the present obscure problem of the high foetal mortality in diabetic pregnancy.

I acknowledge my indebtedness to Mr. John Peel, who was not only responsible for the obstetric management of these cases but also played a large part in the collection and analysis of the questionary series. I am grateful to Dr. R. D. Lawrence for access to the records of his private patients.

REFERENCES

Gilbert, J. A. L., and Dunlop, D. M. (1949). *British Medical Journal*, 1, 48.
Lawrence, R. D., and Oakley, W. (1942). *Quart. J. Med.*, n.s. 11, 45.
Pederson, F. (1949). *Trans. XIIth Brit. Congr. Obstet. Gynaec.*, p. 186. Austral Press, London.
Peel, J., and Oakley, W. G. (1949). Ibid., p. 161.
Smith, G. van S., and Smith, O. W. (1938). *Amer. J. Obstet. Gynec.*, 36, 769.
White, P. (1947). *Penn. med. J.*, 50, 705.

FATAL HYPOGLYCAEMIA IN A DIABETIC PATIENT WITH PITUITARY NECROSIS

BY

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Pituitary necrosis, not associated with shock or haemorrhage, is occasionally encountered in post-mortem examinations. Plaut (1952), in a routine series of necropsies, found pituitary necrosis in 13 out of 149 cases, but does not correlate these findings with clinical findings. Kraus (1920, 1926a, 1926b) noted the relative frequency with which pituitary necrosis is found in diabetics, and particularly in young diabetics, and described certain "diabetic changes in the hypophysis." Kiyono (1926) could find no characteristic changes in the pituitary glands of diabetics, but described two cases in which there was necrosis. Another two cases of pituitary necrosis in young diabetics were reported by Baló (1923).

When pituitary insufficiency complicates diabetes mellitus, conditions exist analogous to those in the Houssay animal. Houssay (1936) showed that diabetes produced in an animal by pancreatectomy was alleviated by subsequent hypophysectomy. Such an animal was readily rendered hypoglycaemic by fasting, and showed pronounced hypersensitivity to insulin.

This phenomenon has been observed in the human subject on a few occasions. Apart from a brief reference by Calder (1932) to a case of Simmonds's disease which showed amelioration of pre-existing mild diabetes, nine cases have been reported (Lyall and Innes, 1935; Kotte and Vonderahe, 1940; Feldman *et al.*, 1947; Vandenbroeck and Férin, 1947; Bastenie, 1949 (quoted by Poulsen, 1953); Marzullo and Handelsman, 1951; Williams, 1952; Israel and Conston, 1952; Poulsen, 1953). The ages of these nine cases (three male, six female) ranged from 29 to 53, with an average of 39. Three cases showed a great improvement in the diabetes (including, in Poulsen's case, disappearance of diabetic vascular lesions in the eye) and remained alive. In each case there was clinical evidence of pituitary damage. Of the six fatal cases necropsy was performed in five, and pituitary necrosis found in every case. In the sixth case there was clinical evidence of pituitary insufficiency. In all the fatal cases there was a disappearance of signs of diabetes of either gradual or sudden onset, and in five of the cases death was associated with marked hypoglycaemia. In the remaining case the blood sugar was not estimated.

Irradiation of the hypophysis, leading to amelioration of diabetes, has been reported by Merle (1935) and by Balfour and Sprague (1949). Similar results following surgical removal of the hypophysis have been reported by Chabanier *et al.* (1936) and by Luft *et al.* (1952).

Another case of pituitary insufficiency in a diabetic is here reported.

Case Report

The patient, a man aged 36 at his final illness is 1952, had no illnesses of importance in childhood, and his development was quite normal. In 1933, at age 17, he was admitted to hospital in diabetic coma. After treatment he was maintained on a diet and insulin, and remained well until 1940, when he was admitted to hospital in hypoglycaemic coma. He responded to treatment with glucose, and thereafter the diabetes was controlled by three daily injections of soluble insulin. In November, 1951, he was admitted to hospital after having been knocked down by a vehicle while in a hypoglycaemic state. He was dismissed, apparently in good health, on a diet of 212 g. of carbohydrate (2,352 calories) and two injections of soluble insulin a day—40 units in the morning, and from 25 to 30 units in the evening.

He seems to have been free of symptoms and regularly at work until April 29, 1952, when he complained of headache and nausea. He took his food and insulin as usual, and went to bed at 11.30 p.m. Two hours later he was found in coma and having convulsions. He was given sugar orally, and he recovered. Throughout that day he remained well, but at 10.15 p.m. he was seen to be acting as though drunk, and an hour later was again comatose and sweating profusely. Oral sugar revived him. Next day he felt well and took his food and usual insulin. At 10 p.m. he was seen staggering along the road, and at 11 p.m. was found completely comatose. He was given sugar by mouth, and at 12 midnight he was sitting up in bed talking and smoking. He had some tea to drink containing 12 teaspoonfuls of sugar. He did not take any more insulin. Two hours later, at 2 a.m. on May 2, he was once again comatose and having convulsions. It was found to be impossible to give him anything by mouth. At 9 a.m. his doctor gave him 50 ml. of 50% glucose intravenously, and 50 ml. of 10% glucose subcutaneously. This had no effect. He was admitted to the Victoria Infirmary at 1 p.m., having then been in coma for 11 hours.

On admission he was seen to be slimly built, but well nourished. He was completely comatose and was sweating profusely. His limbs were spastic, and irregular twitching movements were present. Plantar responses were extensor. Pupils were equal and reacted to light. There was nothing abnormal in the chest or abdomen. Axillary and pubic hair showed normal distribution.

Treatment and Progress

Blood was withdrawn for sugar estimation, and 100 ml. of 50% glucose was given intravenously. No change occurred in his condition. Intravenous glucose was repeatedly administered throughout the afternoon until a total of 300 g. had been given. The blood sugar on admission was 8 mg.

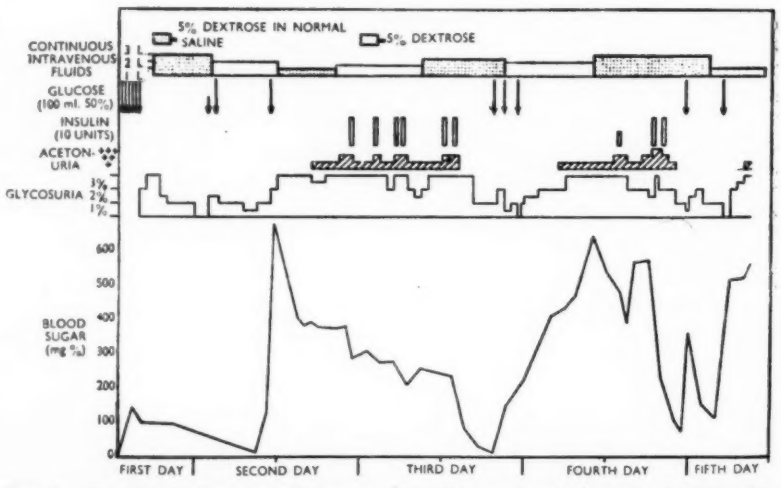

FIG. 1.—Showing intravenous therapy and insulin treatment, degrees of acetonuria and glycosuria, and blood-sugar levels.

per 100 ml. After one and a half hours this had risen to 148 mg., but the patient showed no improvement. Periodic convulsive attacks lasting 10 to 15 minutes occurred, separated by periods of relative calm lasting 24 to 40 minutes. At 4 p.m. a catheter was inserted and, from this time, frequent analyses of urine were made. Blood-sugar estimations were carried out regularly. At 6 p.m. continuous intravenous fluid was started, beginning with 5% dextrose in normal saline. Penicillin, 1,000,000 units, was given, followed by 500,000 units twice daily. Later in the day the convulsions became less severe, but generalized twitching movements persisted. At no time did he respond to cutaneous or aural stimuli.

May 3.—Throughout the day the patient's condition remained unchanged. The skin was moist and twitching movements were still present. Overnight the blood sugar had fallen to severe hypoglycaemic levels (11 mg. per 100 ml.), but subsequently rose and was maintained at between 300 and 400 mg. per 100 ml. Lumbar puncture was performed at 11 a.m.

May 4.—There was no improvement in his clinical state. A heavy glycosuria persisted, and on account of the appearance of ketonuria, increasing in amount, 10-unit doses of soluble insulin were given, up to a total of 60 units. The blood sugar, which throughout the earlier part of the day was maintained at between 200 and 300 mg. per 100 ml. suddenly fell to extremely low levels (14 mg.) with disappearance of ketonuria and glycosuria. Glucose, 150 g. was administered intravenously. The blood sugar then rose to between 100 and 200 mg. Lumbar puncture was repeated at 3.30 p.m.

May 5.—The patient's condition was still unchanged. During the afternoon twitching movements became less marked, and by 6 p.m. were no longer present. Hyperventilation developed and acetone appeared in the breath. Glycosuria and ketonuria increased, and the blood sugar rose to 651 mg. In spite of this hyperglycaemia, sweating remained profuse. Small doses of insulin up to a total of 25 units were again given, resulting in a fall of blood sugar to 78 mg.

May 6.—The limbs were now flaccid. Sweating was still occurring. The blood-sugar levels fluctuated between 118 and 561 mg. per 100 ml. The patient died at 11.10 a.m.

During this period in hospital there was an irregular pyrexia, with a terminal rise to 104.4° F. (40.2° C.). The blood pressure was maintained at about 115/75 until two hours before death, when it fell to 90/50.

The biochemical findings in blood and C.S.F. are summarized in Tables I and II. The fluctuations in blood-sugar readings, with details of therapy, are shown in Fig. 1. The Wassermann reaction of the blood and C.S.F. was negative.

TABLE I.—*Biochemical Findings in the Blood*

Date and Time	Urea (mg./100 ml.)	Chlorides (mg./100 ml.)	Alkali Reserve (Vol. CO_2%)	Potassium (mg./100 ml.)	Calcium (mg./100 ml.)	Phosphorus (mg./100 ml.)	Alkaline Phosphatase (K–A Units)
2/5/52 4 p.m.	46	416	48·1	18·9	—	—	—
3/5/52 11 a.m.	27	591	52·8	—	—	—	—
4/5/52 1.30 p.m.	39	627	45·3	18	9·7	1·15	8·2

TABLE II.—*Biochemical Findings in the C.S.F.*

Date and Time	Glucose (mg./100 ml.)	Chlorides (mg./100 ml.)	Protein (mg./100 ml.)	Cells (per c.mm.)	Granulocytes (%)	Lymphocytes (%)
3/5/52 11 a.m.	80	749	44	35	80	20
4/5/52 3.30 a.m.	208	767	54	23	76	24

Necropsy Report

Necropsy was carried out, four hours after death, by Dr. J. E. Craik, of the Department of Pathology, Victoria Infirmary. There was no evidence of bruising of the scalp or of an old fracture of the skull. The C.S.F. was increased in amount but was clear. There was oedema of the brain with flattening of the convolutions and a slight pressure cone on the inferior surface of the cerebellum, but not on the medulla or pons. The cerebral blood vessels were unusually healthy for a diabetic: they were thin and did not contain any plaques of atheroma. The brain weighed 1,510 g. The cut surface was moist, but there were no petechiae or larger haemorrhages. No softenings or macroscopic abnormalities could be found.

FIG. 2.—Low-power view of pituitary, showing two areas of necrosis. (H. and E. ×7.)

The respiratory, circulatory, digestive, and genito-urinary systems showed no macroscopic abnormalities. The pancreas weighed 55 g.

The suprarenal glands were much enlarged, the right weighing 12 g. and the left 10.5 g. On section it was seen that they had undergone simple hyperplasia, the proportions of cortex and medulla being normal. The pituitary and thyroid appeared normal.

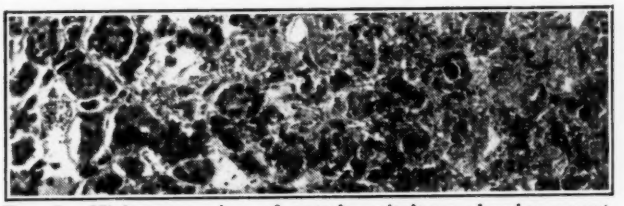

FIG. 3.—High-power view of anterior pituitary, showing recent necrosis to the right and normal pituitary cells to the left. Outlines of necrotic cells are still preserved, but nuclei are small and pyknotic, and the cytoplasm is losing its specific staining reactions. (H. and E. ×100.)

Histology.—In the pancreas, islets of Langerhans were extremely scarce; in a search through two blocks of tissue only one islet was found. It was probably a little on the large size, but otherwise appeared normal. The thyroid showed histological evidence of hyperfunction. The acini varied greatly in size, some being so small as to be almost solid. They were lined by thick cubical epithelium, which was often folded. Colloid was well coloured but did not fill the acini completely, and often there was peripheral vacuolation. Both suprarenals were large, but the hyperplasia was proportional in the medulla and all the layers of the cortex. There was no histological abnormality. The pituitary showed peculiar patchy necrosis in the most anterior part of the anterior lobe. The necrosis was early;

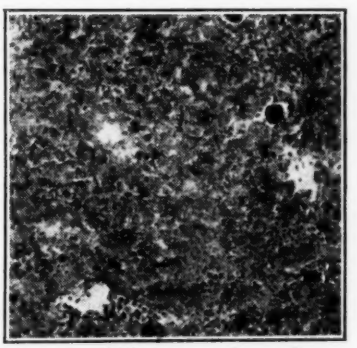

FIG. 4.—High-power view of anterior pituitary, showing older necrosis with gross granulocytic and lymphocytic infiltration. The architecture of the pituitary is almost completely destroyed. (H. and E. ×100.)

in some patches the cells were still well preserved but had pyknotic nuclei; in some the cells were only just discernible; and in others the cells were lost, but the general architecture of the pituitary was still preserved (see Figs. 2, 3, and 4). It was thus obvious that the various patches of necrosis were not of the same age, though none was of more than a few days' duration. In the brain, sections from the pons showed various degrees of degeneration of ganglion cells. A few appeared normal. Most showed moderate or severe chromatolysis up to complete loss of nuclei. Shrinkage of ganglion cells was a feature, most being surrounded by a clear zone. There was no evidence that glial proliferation had begun. In the liver, glycogen was increased, as was to be expected. Otherwise the histological appearances were normal.

Comment

The notable feature of this case is the sudden development of a series of severe hypoglycaemic episodes in a diabetic patient who seems to have been under at least moderately satisfactory control for 19 years. The last of these episodes, which terminated in coma lasting four and a half days and death of the patient, began two hours after he had been treated successfully for an insulin reaction, and in spite of the fact that additional glucose, but no insulin, was given. In hospital, extremely large doses of glucose were required to raise the blood-sugar level, which, however, fell spontaneously to a severe hypoglycaemic level. Later, when small doses of insulin were given to combat ketosis, the blood sugar fell to unexpectedly low levels even while glucose was being administered by intravenous drip. This state of affairs suggests suddenly acquired extreme insulin sensitivity, and the explanation for this may lie in the pathological changes found in the pituitary.

Death in this case resulted from extended hypoglycaemia. Since the brain can utilize only glucose for its metabolism, if this is virtually absent from the blood for a considerable period irreversible changes may be expected in the brain cells. These changes have been studied by Baker and Lufkin (1937), Baker (1938), Sahs and Alexander (1939), and Lawrence, Meyer, and Nevin (1942). The duration of hypoglycaemia required for these changes is not known exactly, although Lawrence *et al.* state that hypoglycaemic coma of one to three hours is compatible with recovery. In the above case the patient had been in coma for 11 hours before admission, and remained in coma despite the rise of blood sugar. Cellular changes in the brain similar to those reported by these observers were, in fact, present.

Summary

Pituitary necrosis is occasionally encountered in routine necropsies. Its occurrence in diabetic subjects is noted.

The Houssay phenomenon is described, and cases are cited of this phenomenon occurring in man.

Irradiation of the hypophysis and hypophysectomy as a treatment of diabetes is mentioned.

Another case of pituitary insufficiency in a diabetic is reported.

Extended hypoglycaemia as the ultimate cause of death is discussed.

I wish to thank Dr. Ian Murray, of the Department of Metabolic Diseases, Victoria Infirmary, for his help and encouragement in the preparation of this article, and for his permission to publish this case; also the staff of the Department of Biochemistry, and Mr. Grey, of the Photographic Department, for their assistance.

REFERENCES

Baker, A. B. (1938). *Arch. Path.*, **26**, 765.
—— and Lufkin, N. H. (1937). Ibid., **23**, 190.
Balfour, W. M., and Sprague, R. G. (1949). *Amer. J. Med.*, **7**, 596.
Baló, J. (1923). *Beitr. path. Anat.*, **72**, 599.
Bastenie, P. A. (1949). Quoted by Poulsen (1953).
Calder, R. M. (1932). *Bull. Johns Hopk. Hosp.*, **50**, 87.
Chabanier, H., Puech, P., Lobo-Onell, C., and Leiu, E. (1936). *Presse méd.*, **44**, 986.
Feldman, F., Roberts, J. B., Susselman, S., and Lipetz, B. (1947). *Arch. intern. Med.*, **79**, 322.
Houssay, B. A. (1936). *New Engl. J. Med.*, **214**, 961.
Israel, S. L., and Conston, A. S. (1952). *J. Amer. med. Ass.*, **148**, 189.
Kiyono, H. (1926). *Virchows Arch. path. Anat.*, **262**, 149.
Kotte, J. H., and Vonderahe, A. R. (1940). *J. Amer. med. Ass.*, **114**, 950.
Kraus, E. J. (1920). *Virchows Arch. path. Anat.*, **228**, 68.
—— (1926a). *Z. Hals-, Nasen- u. Ohrenheilk.* **14**, 142.
—— (1926b). In F. Henke and O. Lubarsch's *Handbuch der speziellen pathologischen Anatomie*, **8**, 810. Berlin.
Lawrence, R. D., Meyer, A., and Nevin, S. (1942). *Quart. J. Med.*, **11**, 181.
Luft, R., Olivecrona, H., and Sjögren, B. (1952). *Nord. Med.*, **47**, 351.
Lyall, A., and Innes, J. A. (1935). *Lancet*, **1**, 318.
Marzullo, E. R., and Handelsman, M. B. (1951). *J. clin. Endocr.*, **11**, 537.
Merle, E. (1935). *Bull. Soc. méd. Hôp. Paris*, **51**, 35.
Plaut, A. (1952). *Amer. J. Path.*, **28**, 883.
Poulsen, J. E. (1953). *Diabetes*, **2**, 7.
Sahs, A. L., and Alexander, L. (1939). *Arch. Neurol. Psychiat., Chicago*, **42**, 286.
Vandenbroeck, J., and Férin, J. (1947). *Ann. Endocr., Paris*, **8**, 366.
Williams, F. W. (1952). *Diabetes*, **1**, 37.

FRIEDREICH'S ATAXIA COMBINED WITH DIABETES MELLITUS IN SISTERS

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The combination of Friedreich's ataxia with diabetes mellitus in families has been mentioned mainly in Continental literature. Schlezinger and Goldstein (1940), in the only comprehensive survey in the English language, list 18 patients from the literature with two of their own. The comparative rarity of the association prompts us to record its occurrence in two sisters.

Case 1

A woman aged 28 was admitted to hospital on September 15, 1950. She had been a full-term normally delivered infant. During her childhood her family noticed that she tended to stumble, to walk on her toes, and to be unable to play or skip normally. The stumbling increased, until at the age of 14 she could just walk along a narrow passage by supporting herself with her hands on the walls, and at this time she could not sit upright in a chair. From the age of 22 she had been partly confined to bed, being able to get around only by holding on to objects in her room, and from 27 she had been wholly bedridden. In 1948 she had been investigated for joint pains and was found to have diabetes mellitus. She was put on a diet without insulin, to which she had since adhered. Menstruation had been scanty, only two to three days every three months, following menarche at 16.

Physical Examination.—The patient sat slumped in a chair and was unable to walk even with assistance. No abnormal signs were found in the heart, lungs, or abdomen. The blood pressure was 108/80. *Skeletal system:* Scoliosis and bilateral pes cavus were present. *Central nervous system:* The patient was fully co-operative. Well-marked head-nodding, particularly during questioning, slurred and slow speech, and coarse lateral and rotary nystagmus were noted. The pupils were equal and reacted briskly to light and on accommodation. The fundi were normal. Right eye 6/12, left 6/6. Colour vision was normal. Other cranial nerves were normal. The upper limbs showed gross hypotonia, ataxia, dysmetria, dysdiadochokinesia, intention tremor, and diminished power, particularly of grip. The biceps, triceps, and supinator jerks were present and equal, though diminished, and there was no wasting or sensory change apart from absent postural sensibility of the fingers. The legs showed hypotonia, incoordination, dysmetria, and

ataxia. Knee- and ankle-jerks were absent, plantar responses extensor. Postural and vibration sense were absent in lower limbs. *Endocrine system:* The pubic and axillary hair normal, no facial hirsuties. There was no abnormal pigmentation. Breast development was normal. The thyroid was of normal size. The reproductive organs were hypoplastic.

Investigations.—The urine contained sugar but no acetone or albumin. On a 140-g. carbohydrate diet and 38 units of soluble insulin morning and evening, blood sugars after a 40-g. breakfast were: 8 a.m., 163 mg.; 10 a.m., 135 mg.; 12 noon, 120 mg. per 100 ml. The fasting blood sugar (receiving insulin) was 140 mg. per 100 ml. A chest radiograph showed normal lung fields and heart shadow. A radiograph of the skull showed a normal sella. Electrocardiograph: Sinus rhythm, 100 a minute; standard leads showed left axis deviation; P–R interval 0.1 second, QRS 0.08 second, T2 flat, T3 inverted, ST3 0.5 mm. depression; leads V4 and V6 showed low-voltage and notched T waves. The serum Wassermann reaction was negative; serum sodium, 300 mg. per 100 ml.; blood cholesterol, 85 mg. per 100 ml. The basal metabolic rate was within normal limits. Cerebrospinal fluid: Normal pressure, normal chemistry and cytology; Wassermann reaction, negative. The 17-ketosteroids were normal, 13 mg. per 24 hours.

Case 2

A woman aged 26, a sister of Case 1, was admitted to the same hospital on February 6, 1951. Schooling had been normal until the age of 13. She had had scarlet fever at 7. After this she had begun to stumble like her sister, to be unable to skip, and to walk on her toes, so that her shoes became worn beneath them. At 19, after an influenzal illness, she was no longer able to walk without help. Her symptoms progressed without remission until the year before admission, from which time she had been confined to her bed, although able to walk with assistance. Two years previously she had been losing weight and her doctor had discovered sugar in her urine. She had been stabilized on insulin with diet. Her menstruation was normal, with menarche at 15.

Physical Examination.—Although confined to bed during the previous year, she was able to walk with aid or with a walking-machine. No abnormal signs were found in the heart, lungs, or abdomen. The blood pressure was 110/85. Lower limbs showed acrocyanosis. *Skeletal system:* Pes cavus on right was present. *Central nervous system:* She was less affected by ataxia than her sister and was brighter mentally. There were oscillating movements of the head and restless movements of the arms, and nystagmus with coarse component to the right. Pupils were equal and reacted briskly to light and on accommodation. Other cranial nerves were normal. The fundi were normal; right eye 6/18, left 6/6. Colour vision was normal. The upper limbs showed hypotonia, dysmetria, and dysdiadochokinesia. The right biceps-jerk was diminished. There were no wasting and no sensory changes. The lower limbs showed weakness without wasting, hypotonia, absent knee- and ankle-jerks, and bilateral extensor plantar responses. Weakness was more marked in the proximal segments; the grip and ankle movements were fair, shoulder and hip movements weak. Vibration sense was absent at the ankles, but other forms of sensation were normal. *Endocrine system:* The pubic and axillary hair were normal; no facial hirsuties. There was no abnormal pigmentation. Breast development was normal. The thyroid was of normal size. The reproductive organs, though hypoplastic, were more developed than her sister's.

Investigations.—The urine contained sugar but no acetone or albumin. On a 100-g. carbohydrate diet with 35 units of soluble insulin morning and evening, blood sugars after a 30-g. carbohydrate breakfast were: 8 a.m., 215 mg.; 10 a.m., 150 mg.; 12 noon, 140 mg. per 100 ml. Fasting blood sugar (receiving insulin) was 180 mg. per 100 ml. A radiograph of the chest showed normal lung fields and heart shadow. A radiograph of the spine showed no spina bifida. The serum Wassermann reaction was negative. Electrocardiograph: Sinus rhythm 100 a minute; low voltage QRS complexes, P–R interval 0.12 second; T waves—changes in all leads, particularly diphasic in T1 and T2, inverted aVL flat in V_6. A radiograph of the skull showed the sella, though small, to be within normal limits. The serum sodium was 315 mg. per 100 ml.; blood cholesterol, 206 mg. per 100 ml. The basal metabolic rate was within normal limits. Cerebrospinal fluid: normal pressure, normal chemistry, and cytology; Wassermann reaction negative. The 17-ketosteroids were normal, 10 mg. per 24 hours.

Family History

Among the patients' parents and their siblings there was no history of clumsiness of gait, foot deformity, twisted spine, or diabetes. III(4), III(6), and II(3) (see Fig. 1) were found to be free from neurological disorder, glycosuria, and

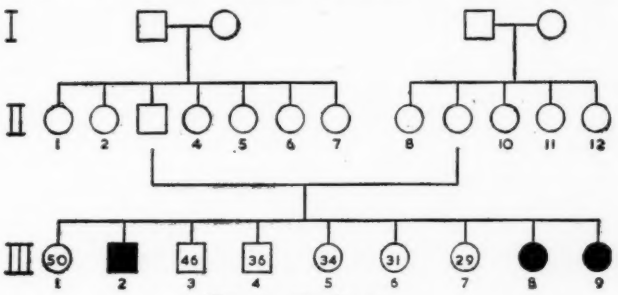

FIG. 1.—Family tree.

congenital deformities. The urines of III(1), III(5), and III(7) did not reduce Benedict's reagent. The eldest brother, III(2), is stated by the sisters to have had a nervous disease similar to their own and to have died from the effects of diabetes at the age of 31. Records of his death have not been available. There was no consanguinity between their parents. Information about the grandparents was scanty.

Recorded Cases of the Combination

Since Schlezinger and Goldstein's paper Segall (1948) has described diabetes in taste-blind identical twins, one of whom had a peculiar dragging walk; both had pes cavus and gradually developing muscular incoordination. Although

FIG. 2.—Photograph of the two sisters. Case 1 is on the right.

the diagnosis of Friedreich's ataxia was not made in these twins, it seems reasonable to suppose that this was in fact the diagnosis. Dassen, Soto Romay, and Fustinoni (1939), have described two cases, not included in Schlezinger and Goldstein's review. Further mention of the combination comes from Bell (1939), who records one patient and a sibling with Friedreich's ataxia, not previously recorded, and from Richards (1946), who described three patients with Friedreich's ataxia in one family, of whom two were diabetic, both males. The present pair brings the total to 29 patients, 20 being females, one pair of these being twins. They are members of the seventh family to be recorded.

Onset of Ataxia and Diabetes

The onset was usually in the first two decades of life, and the Friedreich's ataxia has always preceded the diabetes, which began acutely, requiring insulin for its control or leading to death. However, one of the patients described by Schloss (1932) had merely glycosuria after a high carbohydrate diet, while Mollaret's (1929) patient had only a single episode of severe diabetes mellitus, leading to coma, then subsiding, ultimately requiring no treatment.

Pathogenesis

Schlezinger and Goldstein discuss, apart from coincidence, theories of hereditary predisposition, chromosome linkage, diabetic myelopathy, and neurogenic diabetes.

Coincidence

That the association of Friedreich's ataxia with diabetes mellitus is more than a chance coincidence has been claimed by Curtius, Störring, and Schönberg (1935), and re-emphasized, though with little further evidence, by Schlezinger and Goldstein. A demonstration that the incidence of diabetes mellitus is greater in people with Friedreich's ataxia than in the general population would rule out coincidence. The former authors give the estimated incidence of Friedreich's ataxia in Switzerland as 1 in 90,000. If the incidence were the same in this country there would be about 400 to 500 cases. Taking the total number of diabetics as 150 to 200,000 (Lawrence, 1944)—an incidence of about 1 in 250—one might perhaps expect two of the cases of Friedreich's ataxia to have diabetes mellitus. There is no way of confirming these estimates, but Bell (1939) lists 846 cases of Friedreich's ataxia and hereditary spastic paraplegia (which may be due to a similar genetic fault), including five cases of the combination with diabetes. This is a somewhat higher incidence of diabetes than in the general population, although the numbers involved are small and are a highly selected group.

The most striking thing about the Friedreich's ataxia and diabetes mellitus combination is that the diabetes occurs only in those members of the affected families who have ataxia. There are five members of the sibships concerned who have ataxia alone. The recorded incidence of diabetes then is evidently more in the ataxics than in the other members of the family. It is not known how far the various authors looked for diabetes in the families of patients having Friedreich's ataxia by itself. Curtius *et al.* investigated 41 out of 51 relatives of their two patients with the combination, and found evidence of neither diabetes nor neurological disorder among them. The incidence of status dysraphicus, comprising such conditions as enuresis, funnel-shaped sternum, kyphoscoliosis, asymmetry of breasts, contracture of little finger, pes cavus, spina bifida, acrocyanosis, lumbarization of first sacral vertebra, and cleft palate, was, however, higher than in random samples of the population.

Chromosome Linkage and Genetic Factors

Juvenile diabetes is thought to be inherited as a recessive, though the frequency of manifestation is low in those with appropriate constitution (Gates, 1946). Bell and Carmichael (1939) state that approximately two-thirds of their cases of ataxia were inherited as recessives. If linkage occurs two types of sibships should result : (1) three normal siblings to one with both diseases, and (2) two normal siblings to one with ataxia and one with diabetes. The second type should be three times as common as the first. Most of the reported sibships containing diabetes and ataxia are of the first type, though some also contain one or more cases of ataxia alone, which could be explained on the basis of failure of manifestation of the diabetes. Sibships of the second type seem very uncommon. There are none in Bell and Carmichael's series, and it seems unlikely that diabetes has been missed in the family histories, as it is such a striking disease to the relatives. Moreover, in the pedigree of Curtius *et al.* the histories of 96 members were elicited, 41 out of 51 living members being examined and no diabetes being found.

The lack of sibships with individuals showing one condition or other, and not both, also tells against a hypothesis of looser linkage with cross-overs.

There are three other possibilities to be considered : (1) the ataxia gene may occasionally give rise to diabetes ; (2) there may be two separate genes, one giving rise to ataxia only, the other giving ataxia and diabetes ; and (3) the ataxia gene may express itself in different ways according to the genetic pattern of its environment.

The first possibility does not explain multiple cases of diabetes and ataxia in the same sibship. It would be supported if a high percentage of subclinical diabetes could be found in ataxic families without manifest diabetes. With regard to the second hypothesis, it is known that there are at least three different genetic types of ataxia—dominant, recessive, and sex-linked recessive (Bell and Carmichael). There is no definite proof that these three types are each due to a single gene. Ataxia combined with diabetes may well be a hereditary syndrome due to a gene different from that of recessive ataxia ; the combination of these two diseases may represent the fully developed syndrome, ataxia alone being a milder form with failure of manifestation of the diabetes. This would explain the occurrence of both diseases in one or more members of a sibship and ataxia alone in another. The third possibility is attractive because it would link diabetes with some of the other dysbiotrophies mentioned later and would also effectively explain the multiplicity of cases of diabetes and ataxia within the one sibship. Both diabetes and other dysbiotrophies could result from the effect of certain genetic environments on the ataxia gene. For instance, retinitis pigmentosa has been reported as occurring in the siblings affected by ataxia in two different families (Claus, Frenkel, and Dide, quoted by Alpers and Waggoner, 1929).

Neurogenic Diabetes

No neurogenic lesion causing permanent diabetes has been described. Claude Bernard (1855) produced transient hyperglycaemia by puncture of the fourth ventricle, stimulation of the posterior part of the hypothalamus having a similar transient effect. Stimulation of the ventro-medial nucleus also causes hyperglycaemia, while destruction of these nuclei protects the animals from diabetes normally produced by pancreatectomy (Le Gros Clark *et al.*, 1938). Clinically, such conditions as basal meningitis, cerebral haemorrhage, trauma, and neighbourhood tumours may all produce transient hyperglycaemia, but not permanent diabetes. Friedreich's ataxia does not produce irritative neurological phenomena, and it is difficult to see how a degenerative lesion of the above-mentioned hypothalamic nuclei could cause a diabetes presenting clinically as what Lawrence (1951) calls the "insulin-deficient type." Further evidence against the concept of neurogenic diabetes is afforded by the lack of correlation between the course of the diabetes, which develops acutely over a few weeks or months, and the slow course of the Friedreich's ataxia. In those patients who died in coma there is no report of any dramatic increase in signs of damage to the central nervous system. Moreover, other symptoms of hypothalamic disturbance, such as changes in sleep rhythm, polyphagia, hyperthermia, hyperhidrosis, diabetes insipidus, excessive emaciation, or obesity, have not been described in those cases which have diabetes. Of the 26 patients described in detail, two were physically

underdeveloped and had menstrual irregularity, and three (including our Case 1) showed an infantile uterus with amenorrhoea or oligomenorrhoea. These are the only symptoms which might conceivably be put down to hypothalamic damage. Records of histological examination of brain stem and hypothalamus are scanty. Rossi (1893), quoted by Schlezinger and Goldstein, described areas of degeneration subcortically, including the basal ganglia; and Wichtel (1943), cited by the same authors, reported degenerative change in the dorsal vagus and dentate nuclei, but normal basal ganglia and tuber cinereum. Köhne (1941) demonstrated normal supraoptic and paraventricular nuclei. The pituitary gland showed only an excess of eosinophil cells. There is thus little or no positive evidence in favour of the hypothesis of neurogenic diabetes.

Diabetic Myelopathy

As Friedreich's ataxia precedes the onset of diabetes mellitus, and is unlike any recognized neurological complication of it, theories of diabetic myelopathy need not receive serious consideration.

Dysbiotrophy

Endocrine disturbances in Friedreich's disease are almost always due to hypofunction of one or more glands of internal secretion—for example, myoedema, genital infantilism (Curtius *et al.*; Schlezinger and Goldstein). As diabetes can be a manifestation of islet-cell hypofunction, it can be regarded as analogous to these and other non-neurological dysbiotrophies that occur, such as spina bifida, supernumerary digits, etc. The occurrence of some of these conditions, particularly the endocrine disturbances, may be determined by the genetic *milieu* of the ataxia-bearing gene, thus providing cases analogous to those with diabetes mellitus and Friedreich's ataxia.

Summary

Cases of Friedreich's ataxia and diabetes occurring in siblings are described; the previous literature is reviewed and theories of causation are discussed. Of these, the hypothesis that the combination is either a hereditary syndrome or an effect determined by the genetic *milieu* of the ataxia-bearing gene seems most satisfactory.

We are indebted to Dr. C. N. Armstrong for his helpful criticism and suggestions; to Mr. David F. Smith for his report on the pelvic organs; to Dr. A. C. Crooke for his estimation of the urinary 17-ketosteroids; to Miss U. Phillip for help with the genetic aspects of this paper; and to Dr. Julia Bell for reading the manuscript.

ADDENDUM.—Since this paper was submitted for publication Dr. H. A. Dewar has kindly drawn our attention to two further sisters. One, aged 16, has recently been under his care at the Royal Victoria Infirmary, Newcastle-upon-Tyne. She has mild ataxia, optic atrophy, and diabetes mellitus requiring insulin for its control. Her sister died in diabetic coma at the age of 19, and is said to have had ataxia and optic atrophy as well.

REFERENCES

Alpers, B. J., and Waggoner, R. W. (1929). *Arch. Neurol. Psychiat., Chicago*, **21**, 47.
Bell, J., and Carmichael, E. A. (1939). *Treasury of Human Inheritance*, vol. 4, part 3. Cambridge Univ. Press, London.
Bernard, C. (1855). Quoted in Best and Taylor's *Physiological Basis of Medical Practice*, 4th ed., 1945, p. 590. Baillière, Tindall and Cox, London.
Clark, W. E. Le Gros, *et al.* (1938). *The Hypothalamus*. Oliver and Boyd, Edinburgh.
Curtius, F., Störring, F. K., and Schönberg, K. (1935). *Z. ges. Neurol. Psychiat.*, **153**, 719.
Dassen, R., Soto Romay, R., and Fustinoni, O. (1939). *Sem. méd., B. Aires*, **1**, 1256.
Gates, R. R. (1946). *Human Genetics*, p. 546. Macmillan, New York.
Köhne, G. (1941). *Dtsch. med. Wschr.*, **67**, 177.
Lawrence, R. D. (1944). *The Diabetic Life*, 13th ed. Churchill, London.
—— (1951). *British Medical Journal*, **1**, 373.
Mollaret, P. (1929). *La Maladie de Friedreich*. Lahure, Paris.
Richards, C. E. (1946). In E. P. Joslin's *Treatment of Diabetes Mellitus*, 8th ed., p. 572. Kimpton, London.
Schlezinger, N. S., and Goldstein, K. (1940). *N.Y. St. J. Med.*, **40**, 415.
Schloss, J. (1932). *Dtsch. Z. Nervenheilk.*, **125**, 201.
Segall, G. (1948). *J. Hered.*, **39**, 228

TIME OF ERUPTION OF PERMANENT TEETH IN BRITISH CHILDREN IN 1947-8

BY

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The most recent study of the times of eruption of the permanent teeth in British children is the survey made by Ainsworth in 1925. The object of the present paper is to bring the subject up to date, both by the assembly of new data and by the use of modern methods of analysis. Graphical techniques have usually been employed for estimating the mean eruption times of human teeth—for summaries of the data see Schultz (1934), Dahlberg and Maunsbach (1948), and Gödény (1951). Dahlberg and Maunsbach, and Gödény, have based their own analyses upon the observation of Klein, Palmer, and Kramer (1937) that the frequencies of erupting teeth at successive ages follow the normal probability function. The precision of the statistical methods for analysing integral responses of this function has been greatly improved over the past twenty years by the development of probit analysis (see Finney, 1947), and it is now possible to specify the statistical error of the estimates.

This paper is based on the analysis of dental observations made during the course of the Birmingham Anthropometric Survey on 1,427 boys and 1,365 girls attending elementary schools. The children, who ranged in age from 5 to 13 years, were unselected and were drawn from 87 infant, junior, and secondary modern schools representing all types of area in the City of Birmingham.

Survey

Dental Examination.—The children were examined by one observer throughout (E.D.-T.). Examination was made in a good light with a dental mirror and probe. The observations were dictated to a clerical assistant, who recorded the findings on a standard form. Unerupted and extracted teeth were recorded as not present. The number of teeth extracted during the period of eruption will be very small, and will not have affected the analysis materially. A tooth was classified as erupted as soon as the gum was pierced. Clinical observations on the teeth were also recorded, but these have not been analysed in this paper.

Social and Anthropometric Data.—The Birmingham Anthropometric Survey recorded the occupation of either the father or the family's chief wage-earner. This information was coded into the appropriate socio-economic classification of the Registrar-General by reference to the Classification of Occupations. Class I comprises the professional, Class II the intermediate, Class III the skilled, Class IV the semi-skilled, and Class V the unskilled occupations. The development of puberty was assessed and scored on a four-point scale, using a scheme based on the classification proposed by Greulich *et al.* (1942). The age in months was recorded from the school records to the month below—that is, the age reached. The mean eruption times which are presented have not been adjusted for this grouping. At the examination an index number was allocated to each child to identify both the child and its school.

Combination of the Dental and Anthropometric Surveys

The index number allocated to a child in the anthropometric survey was used in the dental survey. This common index number has linked the two surveys and has been the means of associating the information collected in each.

The records of the dental survey were coded into a numerical form suitable for punching into standard 80-column Hollerith cards. The basis of this coding was that each column represented a tooth, and permitted up to 12 subdivisions. One of these was used to represent each of the possible classes of "absent" and "present" teeth, combined with observations on the incidence of caries.

A set of punch cards was prepared by a mechanical "reproducer" from the master cards of the Birmingham Anthropometric Survey to include only the index number, the age, and other coded information, the punches being made only in the first 19 columns. These cards were passed through a "mechanical interpreter" which printed the index number on the card so that it was easily legible. These "reproduced" punch cards were then matched with the coded dental records, and the dental information read from the records was punched into the remaining columns.

The last preparatory procedure was carried out only to facilitate the computing, and consisted in converting the ages, so far recorded in months, into periods of a quarter of a year by grouping them in threes. The different groups were numbered in numerical order—for example, the ages, 060, 061, 062 (in months) were all numbered 01 (first quarter year) and so on. Each group had the number punched mechanically into the cards. The various manual steps in the coding and punching have been verified at each stage.

Statistical

A preliminary tabulation was made of the number of boys and girls in each age group. The number of erupted teeth in each group was then tabulated for each tooth. The probability of observing erupted teeth in each age group was computed from these data. These probabilities were graphed for all the teeth in the right lower jaw. They were transformed into probit values, and these were also graphed. The best-fitting straight line was fitted to these points, and from this line the corrected probit values were read off and transformed into probabilities. These corrected values were plotted on to the original graphs, and were found to smooth the observed data well. These findings indicate that the normal probability function will form the basis of a satisfactory analysis. As an example the probability of finding erupted lower canine teeth at different ages is shown in the Chart, and the smooth probability curve has been fitted in the manner described.

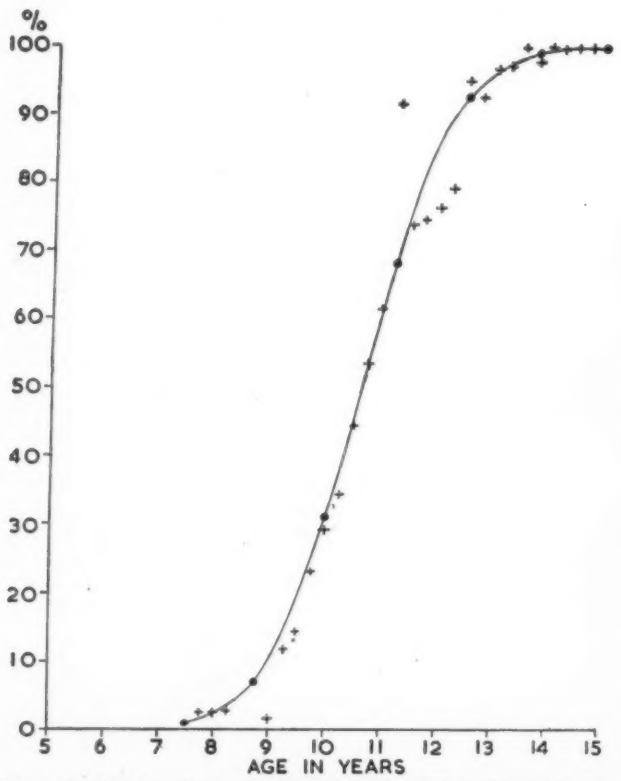

Chart showing the observed probability of eruption of boys' lower right canine teeth at different ages.

The analysis has been made by the probit method. The computations were based on the observed probabilities of finding the teeth erupted at various ages. The technique used was that devised by Black (1950), and the coefficients were corrected for the effects of grouping by the technique of Tocher (1949). Errors of estimate for the various statistics have been computed, and the various tests of significance have been made using a "t" test. There is no evidence of heterogeneity of departure from the fitted probit lines. In the main samples, too, in which the development groups and social classes are pooled, the values of "g" are all less than 0.1, and all except two of them are less than 0.03.

Results

For convenience the following abbreviations have been used in reporting the findings: I_1 for the central incisor tooth; I_2 for the lateral incisor tooth; C for the canine tooth; Pm_1 for the first premolar tooth; Pm_2 for the second premolar tooth; M_1 for the first molar tooth; M_2 for the second molar tooth. No erupted third molar tooth was seen.

Mean Eruption Times of the Teeth.—The data for the teeth of the right upper and lower jaws have been examined in detail, and these form the basis of the various comparisons which have been made. The mean eruption times of the teeth in the upper and lower jaws are given in Table I for both sexes, with the standard error and the 5% and 95% fiducial limits of the mean. The statistics presented in Table I are based on a relatively heterogeneous sample. Thus, children from all classes of the Registrar-General's (1931) socio-economic classifications are included, and in the older age groups adolescents are grouped with children who do not yet show external signs of puberty. The data have been examined to see if these factors influence the mean eruption times of the teeth.

TABLE I.—*Mean Eruption Times, Standard Errors, and the 5% and 95% Limits of the Mean, of the Teeth in the Right Upper and Lower Jaws*

Tooth	Boys				Girls			
	Mean in Months	S.E.	5-95% Limit of Mean		Mean in Months	S.E.	5-95% Limit of Mean	
			Upper	Lower			Upper	Lower
Upper Jaw								
I_1 ..	84·13	0·71	85·52	82·74	79·46	0·57	80·58	78·34
I_2 ..	98·17	0·74	99·62	96·72	93·80	0·87	95·51	92·09
C ..	137·56	0·92	139·37	135·75	128·07	0·85	129·73	126·40
Pm_1 ..	124·96	1·12	127·16	122·76	117·45	0·84	119·09	115·80
Pm_2 ..	138·22	1·13	140·43	136·01	132·76	1·17	135·04	130·47
M_1 ..	73·29	0·78	74·83	71·76	71·25	0·77	72·76	69·74
M_2 ..	143·67	0·94	145·51	141·84	137·94	0·88	139·66	136·22
Lower Jaw								
I_1 ..	72·96	0·72	74·38	71·54	69·22	0·57	70·35	68·08
I_2 ..	87·63	0·71	89·01	86·25	84·17	0·70	85·55	82·79
C ..	126·16	0·80	127·72	124·61	112·90	0·74	114·34	111·45
Pm_1 ..	136·20	0·99	138·14	134·26	126·33	0·94	128·18	124·48
Pm_2 ..	147·87	1·17	150·16	145·57	139·62	1·17	141·91	137·33
M_1 ..	73·69	0·79	75·24	72·15	70·08	0·67	71·40	68·77
M_2 ..	136·87	0·84	138·53	135·22	134·15	0·89	135·89	132·40

Mean Eruption Times of Teeth in Different Social Classes.—The data were sub-classified into the social classes previously specified. Class I was combined with Class II, and Class IV with Class V. Probit computations were carried out on the data for the right lower teeth in boys. None of the differences are statistically significant, although a trend towards an earlier eruption in Classes I and II

TABLE II.—*Mean Eruption Times and Standard Errors of the Teeth in the Right Lower Jaw for Social Classes I and II Combined and for Class III in Boys**

Tooth	Mean Eruption Time in Months with S.E.	
	Social Classes I and II Combined	Social Class III
I_1	68·0±4·9	73·7±0·9
I_2	84·2±1·9	88·3±0·8
C	127·7±3·3	126·4±1·1
Pm_1	133·7±5·0	136·8±1·3
Pm_2	141·0±5·3	148·2±1·5
M_1	73·5±3·1	73·7±1·0
M_2	132·7±4·7	137·2±0·9

* For explanation of classes see text.

combined is apparent. The statistics for Classes I and II combined and for Class III are given in Table II. Classes IV and V combined follow Class III very closely. The mean difference between the classes, over all the teeth, is 3.36 ± 1.13 months, a finding which indicates that the differences between the mean eruption times are important. Further analysis was unprofitable because of the small number of children in Classes I and II.

Variation in Mean Eruption Time Associated with Puberty.—The data were sub-classified into two groups: (1) those showing no onset of pubertal development; and (2) those showing obvious signs of such development. The mean eruption times were computed for the right lower C, Pm_1, Pm_2, and M_2 teeth of boys and girls, and are given in Table III. A trend towards the earlier eruption of teeth

TABLE III.—*Mean Eruption Times and Standard Errors of the Lower Right C, Pm_1, Pm_2, and M_2 Teeth in Boys and Girls With and Without the Physical Signs of Puberty*

Tooth	Boys		Girls	
	Mean Eruption Times in Months with S.E.		Mean Eruption Times in Months with S.E.	
	No Development	With Development	No Development	With Development
C ..	127·7±1·3	123·2±3·7	113·3±0·7	108·9±6·6
Pm_1 ..	137·4±1·6	137·6±2·2	126·8±1·6	124·1±4·4
Pm_2 ..	148·8±1·8	147·8±1·9	136·3±1·7	129·3±8·3
M_2 ..	137·8±1·2	135·3±2·3	133·6±1·1	130·2±2·8

in the pubescent group is apparent in both sexes, although the differences between the mean eruption times are not statistically significant. The mean difference between the two groups, over all the teeth, is 1.95 ± 1.0 months for boys and 4.13 ± 0.72 months for girls; values which indicate that the differences between the mean eruption times of the groups are important. No sub-classification was made into the various stages of puberty, although it was apparent that the few boys and girls who were well advanced all had their M_2 teeth, whatever their age. This observation indicates that if children are examined on several occasions during their growth the early eruption of the M_2 tooth may be found to be associated with early puberty.

The effect of a possible interaction between the social and developmental classifications of the data has been ignored in making these examinations, but the findings indicate that, whilst the mean eruption times of teeth recorded in Table I

TABLE IV.—*Difference in Months Between the Mean Eruption Times with the Standard Error of the Corresponding Right and Left Teeth of the Upper and Lower Jaws*

Tooth	Right and Left Upper Jaw		Right and Left Lower Jaw	
	Boys	Girls	Boys	Girls
I_1 ..	+2·09±1·41	−0·07±0·89	−0·71±1·08	−0·26±0·79
I_2 ..	−0·37±0·95	+0·59±1·27	+0·18±1·03	−0·16±1·01
C ..	+0·70±1·48	−0·97±1·27	+0·12±1·14	+0·07±1·03
Pm_1 ..	−0·34±1·52	+0·99±1·18	+0·88±1·44	−0·02±1·40
Pm_2 ..	−0·56±1·58	−1·92±1·80	+0·31±1·64	−0·67±1·72
M_1 ..	+0·66±1·15	+0·49±1·01	+0.49±1·02	+1·17±0·94
M_2 ..	−0·02±1·26	−0·23±1·24	−1·45±1·30	+1·08±1·28

The mean eruption time of the left tooth has been subtracted from that of the right in all cases.

may apply to elementary schoolchildren generally, because slight variations in the constitution of this population from place to place may be ignored, they should not serve as standards for other groups of children.

Mean Eruption Times of the Dentitions on the Right and Left Sides.—The mean eruption times have been computed for the right and left upper and lower teeth. The differences between these times are set out in Table IV. No significant difference was found between the mean eruption times of the teeth of the right and left sides of the upper and lower jaws in boys and girls.

Sexual Differences in the Mean Eruption Times.—A comparison of the mean eruption times of the teeth in the right upper and lower jaws of boys and girls is given in Table V.

TABLE V.—*Differences Between the Mean Eruption Times, with Standard Errors, of the Teeth of Boys and Girls in the Right Upper and Lower Jaws, and Between the Upper and Lower Jaws in the Same Sex*

Tooth	Right Upper Jaw	Right Lower Jaw	Boys	Girls
	Difference Between the Mean Eruption Times in Months, with S.E.	Difference Between the Mean Eruption Times in Months, with S.E.	Difference Between the Mean Eruption Times in Months, with S.E.	Difference Between the Mean Eruption Times in Months, with S.E.
	Boys−Girls	Boys−Girls	Upper−Lower	Upper−Lower
I_1 ..	+4·67±0·91†	+3·74±0·92†	+11·17±1·01†	+10·24±0·81†
I_2 ..	+4·37±1·14†	+3·46±1·00†	+10·54±1·03†	+9·63±1·12†
C ..	+9·49±1·25†	+13·26±1·09†	+11·40±1·22†	+15·17±1·13†
Pm_1 ..	+7·51±1·40†	+9·87±1·37†	−11·24±1·49†	−8·88±1·26†
Pm_2 ..	+5·46±1·63†	+8·25±1·66†	−9·65±1·63†	−6·86±1·65†
M_1 ..	+2·04±1·10	+3·61±1·04†	−0·40±1·11	+1·17±1·01
M_2 ..	+5·73±1·29†	+2·72±1·22*	+6·80±1·26†	+3·79±1·28†

* Probability of less than 5%.
† Probability of less than 1%.

In the upper jaw the mean eruption time of every tooth with the exception of the M_1 was significantly later for the boys than for the girls. In the lower jaw the mean eruption times of the teeth in boys were significantly later than those for the girls. (The level of significance of the difference in the case of the M_2 tooth is only at the 5% level of probability.) This finding confirms the previous observations made by Ainsworth (1925) and Leslie (1951).

Comparison of the Mean Eruption Times of the Corresponding Upper and Lower Teeth.—The differences between the mean eruption times for boys and girls are given in Table V. It is apparent that the mean eruption times of the teeth in the upper jaw are later for both sexes, with the following exceptions:—Boys: The lower Pm_1 and Pm_2 teeth erupt about 11 and 10 months respectively after the corresponding upper teeth (a difference statistically significant at the 1% level of probability). The difference between the upper and lower M_1 teeth was not significant. Girls: The lower Pm_1 and Pm_2 teeth erupt a matter of nine and seven months respectively after the upper teeth (both differences are statistically significant at the 1% level of probability). The difference between the mean eruption times of the upper and lower M_1 teeth was not significant. The observation that the mean eruption time of the lower Pm_1 tooth is significantly later than that of the upper for boys and girls, whereas generally the teeth in the upper jaw are later than those in the lower jaw, has also been made in previous surveys.

Sequence of the Mean Eruption Times.—The order of eruption of the teeth determined from the mean eruption times is set out in Table VI. It is found that the order is the same in boys and girls, but that the order is different in the upper and lower jaws. The eruption times of the I_1 and M_1 teeth and the Pm_1, Pm_2, and M_2 teeth are so similar that sampling variation can give rise to a different order of eruption in a proportion of determinations. The order of eruption of the teeth has been determined from the mean eruption times found in some recent surveys, and the results are included in Table VI. It is apparent that the

TABLE VI.—*Order of Eruption of the Permanent Teeth in Several Countries, as Determined from the Mean Eruption Times*

Country of Origin:	England				New Zealand		America		Hungary		Sweden	
Tooth	Birmingham Survey		Ainsworth (1925)		Leslie (1951)		Klein *et al.* (1937)		Gödény (1951)		Dahlberg and Maunsbach (1948)	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Upper Jaw												
I_1	2	2	2	2	2	2	2	2	2	2	2	2
I_2	3	3	3	3	3	3	3	3	3	3	3	3
C	5	5	6	6	5	5	6	6	6	5	6	6
Pm_1	4	4	4	4	4	4	4	4	4	4	4	4
Pm_2	6	6	5	5	6	6	5	5	5	6	5	5
M_1	1	1	1	1	1	1	1	1	No data—assumed to be erupted first			
M_2	7	7	7	7	7	7	7	7	7	7	7	7
Lower Jaw												
I_1	1	1	2	2	1	1	2	2	No data—assumed to be erupted first or second			
I_2	3	3	3	3	3	3	3	3	3	3	3	3
C	4	4	4	4	4	4	4	4	4	4	4	4
Pm_1	5	5	5	5	5	5	5	5	5	5	5	5
Pm_2	7	7	6	6	7	7	6	6	6	6	6	6
M_1	2	2	1	1	2	2	1	1	No data—assumed to be erupted first or second			
M_2	6	6	7	7	6	6	7	7	7	7	7	7

anticipated variations in the order resulting from sampling variations have been found, but, apart from this, the order of eruption is the same in each survey.

Discussion

Although the statistical significance of the differences cannot be assessed satisfactorily, comparison of the mean times of eruption of teeth found in this survey with those reported by Ainsworth (1925) suggests that to-day the mean eruption times of teeth are, with the following exceptions, a few months earlier in each sex: the upper and lower Pm_2 teeth in both sexes, the upper and lower Pm_1 teeth in boys, the lower Pm_1 teeth in girls, which are all a few months later than they were 25 years ago. Except in the case of the premolar teeth, the mean eruption times found in 1947–8 also tend to be a few months sooner than those which are indicated by the data for English children published by James and Pitts (1912).

These comparisons suggest that there has been a tendency for the mean eruption times of all teeth, except the premolars, to become earlier in this country during the past 40 years. The later eruption of the premolar teeth may be attributable to a fall in the rate of extraction of the preceding temporary molar teeth, and may be a change towards a more normal time of eruption (see Leslie, 1951). The indications that mean eruption times of teeth, other than the premolars, may be earlier in children from a better socio-economic environment, which are provided by the present survey and which are supported by the observations of Hellman (1923) on the incisor teeth, suggest that this trend may reflect a progressive improvement in the socio-economic condition of the nation. The conclusions Hellman drew from his data were based mainly on the findings for the premolar teeth, and differ from ours on this account.

The likelihood that socio-economic and general physical status have an influence on the time of eruption is given further substance by the observations that children who show physical signs of puberty tend to have earlier mean eruption times than children who are still prepubertal.

The mean eruption times of teeth as determined in the Birmingham Survey appear to be a few months in advance of those found by Leslie (1951) for New Zealand children. The method by which his statistics are computed introduces errors due to rounding, and thus makes the statistical significance of any detailed comparison with our data uncertain, but the differences would probably be statistically significant for about half of the teeth. The mean eruption times of the teeth of Birmingham children tend to be earlier than those of other European children, except for the lower premolar teeth, and the differences are slightly greater than they are in the New Zealand data (Dahlberg and Maunsbach, 1948; Gödény, 1951). These findings suggest that the physical development of British children to-day, in so far as it is reflected in changes in the mean eruption times of teeth, is slightly in advance of that of other children of European stock, and those from New Zealand, about which we have information.

Summary

The mean times of eruption of human teeth have been computed from observations on 1,427 boys and 1,365 girls aged 5 to 13 years.

The mean times of eruption of teeth of children who are either of a superior socio-economic group or are pubescent tend to be earlier than those in other children.

The mean times of eruption of the corresponding right and left teeth do not differ significantly in either the upper or the lower jaws.

The mean times of eruption of the teeth of boys are, with the exception of the upper M_1 teeth, later than those of girls.

The mean times of eruption of teeth in the upper jaw are later than those in the lower jaw, except for the Pm_1 and Pm_2 teeth, which are earlier, and the M_1 teeth, which do not differ significantly.

The order of eruption of the teeth determined from mean eruption times is the same, within the limits of sampling variation, as that found in other stocks of European origin.

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REFERENCES

Ainsworth, N. J. (1925). *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 97.
Black, A. N. (1950). *Biometrika*, **37**, 158.
Dahlberg, G., and Maunsbach, A. B. (1948). *Acta genet., Basel*, **1**, 77.
Finney, D. J. (1947). *Probit Analysis*. Cambridge.
Gödény, E. (1951). *Acta genet., Basel*, **2**, 331.
Greulich, W. W., Dorfman, R. I., Catchpole, H. R., Soloman, C. I., and Culotta, C. J. (1942). *Monogr. Soc. Res. Child. Dev.*, **7**, No. 3, Serial No. 33.
Hellman, M. (1923). *Dent. Cosm.*, **65**, 34.
James, W. W., and Pitts, A. T. (1912). *Proc. roy. Soc. Med.*, **5** (Odont. Sect.), 80.
Klein, H., Palmer, C. E., and Kramer, M. (1937). *Growth*, **1**, 385.
Leslie, G. H. (1951). *A Biometrical Study of the Eruption of the Permanent Dentition of New Zealand Children*. Government Printing Office, Wellington.
Registrar-General (1931). Classification of Occupations. H.M.S.O., London.
Schultz, A. H. (1934). *Amer. J. phys. Anthrop.*, **19**, 489.
Tocher, K. D. (1949) *Biometrika*, **36**, 9.

ORDER OF ERUPTION OF THE PERMANENT HUMAN DENTITION

BY

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Whilst the order of eruption of teeth as determined from mean eruption times is relatively constant (Clements, Davies-Thomas, and Pickett, 1953), the times of eruption of individual teeth are very variable, and consequently individual children may be expected to vary greatly in the order in which their teeth erupt. This is shown by Table I, which provides estimates of the 5% and the 95% limits of the ages of eruption in children examined in the course of the Birmingham Anthropometric Survey. It is also evident from Table I and the Chart that eruption times overlap considerably. The explanation is clearly that the eruption times of each tooth are distributed at random, so that late eruption of a tooth with a relatively early mean eruption time may occur after the early eruption of a tooth with a later mean eruption time.

TABLE I.—*Mean Eruption Times, and the 5 and 95% Limits of Distribution for the Teeth of Boys and Girls in the Right Upper and Lower Jaws*

Tooth	Boys				Girls			
	Mean in Months	S.D.	5–95% Limit of Distribution		Mean in Months	S.D.	5–95% Limit of Distribution	
			Upper	Lower			Upper	Lower
Upper Jaw								
I_1 ..	84·13	9·97	100·48	67·69	79·46	7·65	92·01	66·83
I_2 ..	98·17	10·10	114·74	81·51	93·80	12·40	114·13	73·35
C ..	137·56	16·39	164·44	110·51	128·07	14·85	152·43	103·56
Pm_1 ..	124·96	21·90	160·88	88·83	117·45	14·63	141·45	93·30
Pm_2 ..	138·22	21·74	173·87	102·35	132·76	22·06	168·93	96·36
M_1 ..	73·29	10·91	91·19	55·29	71·25	10·79	88·95	53·45
M_2 ..	143·67	14·93	168·15	119·04	137·94	14·15	161·15	114·59
Lower Jaw								
I_1 ..	72·96	9·38	88·32	57·48	69·22	6·76	80·29	58·14
I_2 ..	87·63	9·71	103·55	71·61	84·17	10·12	100·78	67·47
C ..	126·16	14·71	150·28	101·90	112·90	11·99	132·57	93·11
Pm_1 ..	136·20	19·74	168·76	103·63	126·33	18·87	157·00	95·49
Pm_2 ..	147·87	20·83	182·24	113·70	139·62	21·88	175·51	103·52
M_1 ..	73·69	10·99	91·71	55·67	70·08	8·80	84·51	55·57
M_2 ..	136·87	14·49	160·61	112·93	134·15	13·23	155·85	112·31

I_1 = the central incisor tooth; I_2 = the lateral incisor tooth; C = the canine tooth; Pm_1 = the first premolar tooth; Pm_2 = the second premolar tooth; M_1 = the first molar tooth; M_2 = the second molar tooth.

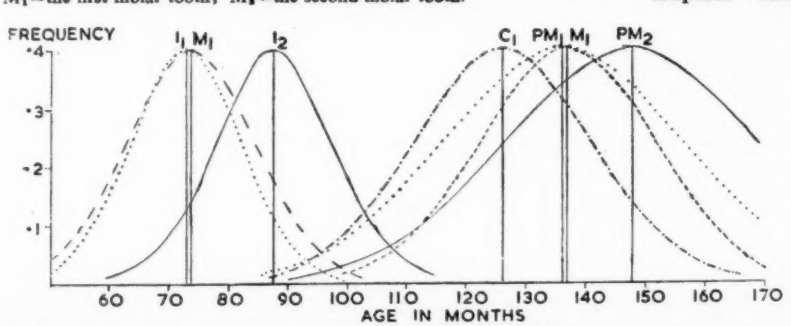

Chart showing standardized frequency distribution of the eruption times of the permanent teeth in the lower jaw for boys.

Little or no variation would be found in the order of eruption if the early eruption of one tooth was associated with the early eruption of the others. Alternatively, if the times of eruption of the various teeth were independent, all possible variations in the order of eruption would occur. The data on tooth eruption collected in the Birmingham Anthropometric Survey were therefore examined to determine whether or not the order of eruption of teeth which have their mean eruption times close together is constant, and, if variations occur, to estimate the probability of different patterns of eruption.

Method

The records of a tooth have been classified as erupted (the tooth having pierced the gum) or unerupted. Each of these classes has been sub-classified into two further classes by sorting the records of another tooth into classes of erupted and unerupted teeth. The records of two teeth comprise the simplest case, and for these a fourfold table may be constructed to indicate the number of occasions on which (1) both teeth were present, (2) neither tooth was present, and (3) either one or the other tooth was present. Additional teeth may be similarly sub-classified to give 16 possible combinations for four teeth. Only the records of children who were of such an age that erupting teeth might be expected to occur have been examined.

TABLE II.—*Occurrence of Erupted and Unerupted I_1 and M_1 Teeth in the Jaws of Children Aged 5–9 Years*

Teeth Erupted	Boys	Girls	Total
Upper Jaw			
I_1	7 (4·7%)	8 (6·6%)	15 (5·6%) χ^2=0·46
M_1	142 (95·3%)	113 (93·4%)	255 (94·4%) (1 d.f.)
Number of occasions when 1 tooth was erupted	149	121	270
Lower Jaw			
I_1	55 (53·9%)	45 (54·2%)	100 (54·0%) χ^2=0·02
M_1	47 (46·1%)	38 (45·8%)	85 (46·0%) (1 d.f.)
Number of occasions when 1 tooth was erupted	102	83	185

Factors which may tend to accelerate or retard the eruptions of certain teeth, such as the early eruption of the premolar teeth following on the early loss of the deciduous teeth, may also affect the frequencies of the orders of eruption (see Leslie, 1951).

Results

The order of eruption of the I_1 and M_1 teeth has been examined in 644 boys and 633 girls aged 5 to 9 years. In each sex the records were divided into a group in which the upper right I_1 tooth had erupted and one in which it had not. The same was done with the lower teeth. Each of these classes was then divided into a subgroup in which the M_1 tooth had erupted and another in which it was still unerupted. The findings are given in Table II. Either one or the other of the two upper teeth was seen alone on 149 occasions in boys and 121 occasions in girls; the corresponding figures for the lower jaw were 102 occasions in boys and 83 occasions in girls; upper I_1 occurred alone seven times in boys and eight times in girls; lower I_1 was seen alone 55 times in boys and 45 times in girls; upper M_1 was seen alone 142 times in boys and 113 times in girls; lower M_1 was seen alone 47 times in boys and 38 times in girls. These proportions are similar for both sexes (χ^2=0.46 and 0.02 (1 d.f.) respectively).

TABLE III.—*Occurrence of Erupted and Unerupted C, Pm_1, Pm_2, and M_2 Teeth in the Jaws of Children 7–14 Years Old.*

No. of Teeth in Group		Classes of Erupted and Unerupted Teeth				Upper Jaw				Lower Jaw			
						Right		Left		Right		Left	
						Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
		C	Pm_1	Pm_2	M_2	No. %	No. %	No. %	No. %	No. %	No. %	No. %	No. %
3 teeth	1	+	+	+	0	75 (57·7)	82 (58·6)	64 (54·2)	86 (53·4)	30 (25·9)	49 (36·0)	30 (27·8)	52 (38·0)
	2	+	+	0	+	33 (25·4)	44 (31·4)	33 (28·0)	54 (33·6)	77 (66·3)	78 (57·4)	72 (66·7)	77 (56·2)
	3	+	0	+	+	8 (6·1)	1 (0·7)	7 (5·9)	1 (0·6)	8 (6·9)	7 (5·1)	5 (4·6)	6 (4·3)
	4	0	+	+	+	14 (10·8)	13 (9·3)	14 (11·9)	20 (12·4)	1 (0·9)	2 (1·5)	1 (0·9)	2 (1·5)
Total ..						130	140	118	161	116	136	108	137
2 teeth	5	+	+	0	0	25 (28·4)	42 (49·4)	38 (37·3)	50 (51·6)	52 (45·2)	72 (67·3)	50 (42·7)	71 (59·7)
	6	+	0	+	0	3 (3·4)	0 (0·0)	3 (2·9)	1 (1·0)	4 (3·5)	5 (4·7)	5 (4·3)	5 (4·2)
	7	+	0	0	+	1 (1·1)	3 (3·5)	5 (4·9)	2 (2·1)	51 (44·3)	28 (26·1)	50 (42·7)	40 (33·6)
	8	0	0	+	+	2 (2·3)	1 (1·2)	1 (1·0)	0 (0·0)	1 (0·9)	0 (0·0)	1 (0·9)	0 (0·0)
	9	0	+	0	+	11 (12·5)	5 (5·9)	6 (5·9)	7 (7·2)	1 (0·9)	0 (0·0)	3 (2·6)	2 (1·7)
	10	0	+	+	0	46 (52·3)	34 (40·0)	49 (48·0)	37 (38·1)	6 (5·2)	2 (1·9)	8 (6·8)	1 (0·8)
Total ..						88	85	102	97	115	107	117	119
1 tooth	11	+	0	0	0	10 (7·5)	8 (7·5)	5 (3·8)	4 (4·2)	74 (71·9)	123 (86·0)	74 (67·9)	118 (89·4)
	12	0	+	0	0	106 (79·7)	82 (77·4)	101 (77·7)	79 (83·2)	13 (12·6)	11 (7·7)	21 (19·2)	6 (4·6)
	13	0	0	+	0	11 (8·3)	10 (9·4)	14 (10·8)	6 (6·3)	7 (6·8)	3 (2·1)	4 (3·7)	4 (3·0)
	14	0	0	0	+	6 (4·5)	6 (5·7)	10 (7·7)	6 (6·3)	9 (8·7)	6 (4·2)	10 (9·2)	4 (3·0)
Total ..						133	106	130	95	103	143	109	132

+=erupted: the tooth has pierced the gum. 0=unerupted. There were approximately equal numbers of children in each age group.

The records of the C, Pm_1, Pm_2, and M_2 teeth have been sorted in a similar way for 1,135 boys and 1,077 girls from 7 to 14 years old, and the results for the right and left upper and lower jaws are given in Table III. This table should be read as in the following example, reading from line 9 of Table III for the right upper jaw: "Two teeth were erupted and two unerupted on 88 occasions in boys. The Pm_1 and M_2 teeth were the erupted teeth on 11 occasions (12.5%). Two teeth were erupted on 85 occasions in girls and the eruption of the Pm_1 and M_2 teeth together was seen five times (5.9%)"; and so on for the left side.

All the combinations of these four teeth have been seen, the combinations varying greatly in their frequency. The differences between the distributions have been tested for significance. The frequencies found in the right and left sides in the same sex do not differ statistically. The difference in the frequencies found between the sexes are all significantly different at the 1% level of probability except for three classes: (1) where three teeth have erupted in the lower jaw; (2) where two teeth have erupted in the lower jaw; and (3) where one tooth only has erupted in the upper jaw. The values of χ^2 for the teeth in the upper and lower jaws respectively, are: for three teeth 6.46 and 14.26 (3 d.f.); for two teeth 22.35 and 13.76 (5 d.f.); for one tooth 23.86 and 0.36 (3 d.f.). The distributions are very different in the upper and lower jaws of the same sex.

The frequencies of the various orders of eruption for different combinations of only two or three teeth out of the four teeth tabulated in Table III may be obtained by combining the appropriate lines of the table so as to omit the tooth not required.

Discussion

The present observations substantiate, what is already well known, that there is considerable variation in the order in which human teeth erupt, and extend this knowledge by providing estimates of the frequencies with which different patterns of eruption may occur in British children.

The most frequent order of eruption of the upper and lower I_1 and M_1 teeth, and the upper and lower C, Pm_1, Pm_2, and M_2 teeth, in both sexes is the same as that given by the mean eruption times. These are: the M_1, I_1, and the Pm_1, C, Pm_2, M_2 teeth in the upper jaw; the I_1, M_1, and the C, Pm_1, M_2, Pm_2 teeth in the lower jaw.

The mean time of eruption of the upper I_1 tooth is later than that of the upper M_1 tooth by 11 months in boys and eight months in girls, and this implies that the distributions of these teeth will overlap only slightly. On the other hand, the mean eruption times of the lower I_1 and M_1 teeth hardly differ in either sex, and so the distributions of these teeth will almost coincide (see Chart). The upper right I_1 tooth was seen to erupt before the corresponding M_1 tooth on 5.6% of occasions, and the lower I_1 tooth on 54.0% of occasions. These observations agree well with the expected values computed from the data of Table I assuming independence. On this assumption I_1 erupts first in 4.0% and 54.8% of all cases in the upper and lower jaws respectively.

Erupted Pm_1, Pm_2, and M_2 teeth were observed without an erupted C tooth 27 times, or on about 10% of occasions, in the right side of the upper jaw, and three times, or on about 1% of occasions, in the right side of the lower jaw. On the assumption that the order of eruption of teeth on the right side is independent of that on the left, both sides will show these three teeth to be erupted on about 1% and 0.1% of occasions in the upper and lower jaws respectively. This condition was observed, however, 13 times in the upper jaw and once in the lower jaw. These observations do not accord with the estimated frequencies, and indicate that the eruption times of corresponding right and left teeth are correlated.

All possible combinations of the orders of eruption of the C, Pm_1, Pm_2, and M_2 teeth actually occur in the Birmingham records. The frequency with which departures occur from the assumed normal order of appearance of the teeth, as given by the mean times of their eruption, implies that the times of eruption of these four teeth are independent of each other.

A similar type of analysis to that undertaken in this study was made by Livy (1885). He compared the eruption times of the corresponding upper and lower teeth in children; he also found that the order of eruption was reversed in a variable proportion of cases in each age group.

It is apparent that many instances of abnormal orders of eruption of teeth which are encountered in the field of orthodontics simply represent extremes of the normal variation; the only sense in which they are abnormal is that they are infrequent.

Summary

The order in which the I_1 and M_1 teeth and the C, Pm_1, Pm_2, and M_2 teeth erupt in British children was investigated and considerable variations were found in both the upper and the lower jaws.

The frequencies of occurrence of the different patterns of eruption were estimated. The most frequent order of eruption was found to be the M_1 tooth followed by the I_1 tooth, and the Pm_1 tooth, followed in succession by

the C, Pm_2, and M_2 teeth in the upper jaw; and the I_1 tooth followed by the M_1 tooth, and the C, Pm_1, M_2, and Pm_2 teeth in that order in the lower jaw.

The analysis indicates that the times of eruption of teeth with similar mean eruption times on the same side are independent of each other, but that the eruption times of corresponding teeth on the right and left sides are correlated.

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REFERENCES

Clements, E. M. B., Davies-Thomas, E., and Pickett, K. G. (1953). *British Medical Journal*, 1, 1421.
Leslie, G. H. (1951). *A Biometrical Study of the Eruption of the Permanent Dentition of New Zealand Children*. Government Printing Office, Wellington.
Livy, J. (1885). *British Medical Journal*, 2, 241.

MAMMARY ABSCESS

DISADVANTAGES OF ANTIBIOTICS IN ITS MANAGEMENT

BY

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In days gone by the cardinal signs of inflammation, heat, pain, redness, and swelling were all too familiar. Just as the classical picture of lobar pneumonia with its typical crisis is seen no more, so the clinical features of acute pyogenic infections have been greatly altered since the general introduction of antibiotics. No one will deny their immense value in combating what were earlier most severe infections, but in less severe cases they can be a mixed blessing if not used with judgment and restraint. The need for surgery is as great as ever, although its extent may be much restricted. Since antibiotics can mask so effectively many of the arresting features of acute infections, the timing of an operation is becoming more and more important.

A good deal of suffering can, in my opinion, be avoided by a general appreciation of the limitations of antibiotics in the treatment of acute infections, and this point I want to underline by citing the records of four cases of acute mammary abscess. Cases of this sort are no doubt the everyday experience of most active general surgeons, but it is their very frequency which has prompted me to record the following cases.

Case 1

The patient was aged 26. Immediately after a normal delivery her left nipple became sore and cracked, and led to weaning. Two weeks later, 24 days after her confinement, she developed a painful swelling in her left breast. On the twenty-ninth day she was seen by her own doctor, who noticed a painful, red, indurated area in the lower half of the left breast. "Distaquaine penicillin," 400,000 units, was given daily, together with local applications of heat for four days. She was admitted to hospital on the thirty-sixth post-partum day, and 12 days after the onset of symptoms.

The left breast was fuller and more pendulous than the right, which seemed quite normal. There was an obvious swelling in the lower and outer quadrant. Peau d'orange was not seen. The nipple was not retracted, but the lower half of the areola was tethered to a hard, slightly tender non-fluctuant mass, measuring 8 by 8 cm., and easily felt by the flat of the hand. The skin over the mass was not discoloured and was no hotter than the surrounding breast tissue. There was some fixity of the mass to the underlying pectoral fascia. Glands were not palpable in the axilla.

When she was first seen in hospital the absence of the signs of inflammation and the size, hardness, and fixation of the mass in the breast strongly suggested the diagnosis of a lactation cancer.

On the following day a radial incision was made over the most prominent part of the mass. A very thick-walled multiloculated abscess cavity was entered, which was involving most of the lower half of the breast. Free drainage was established. The pus yielded a profuse growth of a coagulase-positive *Staphylococcus pyogenes*, resistant to penicillin but sensitive to aureomycin, streptomycin, and chloramphenicol. Streptomycin, 0.5 g., was given twice daily for four days. Two weeks later the wound was completely healed, and there was no more than a diminishing thickening. Her total period of disability was 26 days.

Case 2

The patient, aged 32, noticed pain, tenderness, and swelling in her right breast three days after a normal confinement. For the next ten days she was given daily injections of distaquaine penicillin, 300,000 units, and local applications of kaolin poultices. The swelling became less painful but no smaller. On the twenty-fourth post-partum day the baby had to be weaned, when the patient developed a generalized rash. On the thirtieth day her own doctor again prescribed injections of penicillin of the same dosage as previously because the breast and upper arm had become stiff and swollen.

On admission to hospital on the thirty-fifth day—that is, 32 days after the onset of symptoms—her temperature was 98.4° F. (36.9° C.), pulse 80, respirations 20, and white blood cell count 11,000. She was looking in the very best of health. The left breast was normal. The right breast was enlarged and deformed by a large, easily visible swelling in the right lower quadrant. There was no peau d'orange, but a little reddish discoloration and oedema over the centre of the swelling. The upper part of the areola was tethered to the tumour. The mass was hard, smooth, and slightly tender, non-fluctuant, and a little hotter than the surrounding breast tissue. It was fixed to the underlying pectoral fascia. There were three firm, tender glands in the right axilla. There were even fewer signs and symptoms of an acute inflammatory condition in the breast than in Case 1. The patient was a very healthy-looking woman with no evidence of fever or toxaemia, complaining only of a large, slightly tender mass in her right breast.

The fixity of the mass to the skin, areola, and underlying fascia; the oedema of the breast and the upper arm; and the presence of enlarged glands in the axilla were once again very suggesive of a lactation carcinoma. The next day a radial incision was made over the most prominent part of the mass. A great depth of dense inflammatory tissue had to be penetrated to find one small loculus of pus in its centre. Bleeding was profuse and difficult to control. Culture of the pus yielded a profuse growth of *Staph. pyogenes* resistant to penicillin but sensitive to streptomycin, aureomycin, and chloramphenicol.

A section from the abscess wall showed an inflammatory reaction with infiltration by foamy macrophages, plasma cells, and polymorphonuclear cells. There was an area of fat necrosis.

Streptomycin, 1 g. twice daily, was given for six days. She was discharged on the sixteenth post-operative day with a clean granulating wound but still some residual thickening in the breast.

Case 3

This patient, aged 28, was confined five weeks before coming to hospital, and complained of pain in the left breast for two days immediately prior to admission.

The left breast was diffusely swollen and tender. There was no discoloration or oedema. After eight days of distaquaine penicillin, 300,000 units daily, the breast was indurated in the left upper and outer quadrant, but less tender and still non-fluctuant.

Chloramphenicol, 0.5 g. four times daily, was given for seven days, by which time fluctuation had developed. Exploration revealed a multiloculated breast abscess with a thick and densely hard wall. Brisk bleeding was encountered, and this could be controlled only by packing. Six daily doses of 300,000 units of distaquaine penicillin were then given, the wound being dressed every third day. The patient was discharged on the thirty-fifth day after the onset of symptoms. She returned, however, one month later with a recurrence of symptoms. Distaquaine penicillin, 600,000 units daily, was given for seven days, and then streptomycin, 1 g. a day for a further seven days. The old incision was then reopened, and pus encountered which grew a penicillin-resistant coagulase-positive *Staph. pyogenes*. The patient was discharged with the wound well healed 54 days after the recurrence of symptoms. In all, she had been attending hospital 116 days, with a brief respite in the middle, after first being seen with a simple acute breast abscess.

Case 4

This patient, aged 32, complained of pain and swelling in the right breast on the thirty-first day after her confinement, and came to hospital four days later.

The left breast appeared normal. The right breast was red and swollen, with a very tender, smooth lump measuring 5 by 5 cm. just below the areola.

Stilboestrol, 10 mg. thrice daily, was given for five days, and 5 mg. for a further ten days. At the same time a dose of 600,000 units of distaquaine penicillin was given daily until the tenth day after the onset of symptoms. The lump was then still the same size but distinctly less tender.

On the thirteenth day a large breast abscess was drained. Daily injections of 600,000 units of distaquaine penicillin were continued until the nineteenth day, when the wound was still discharging and a new area of induration and tenderness had appeared above the areola. Two days later a second thick-walled abscess was drained of approximately 5 ml. of pus, which again yielded a penicillin-resistant *Staph. pyogenes*. After a further 17 days the wound was well healed. The patient took 34 days to recover from an acute breast abscess.

Discussion

Cases 1 and 2 serve to illustrate how the symptoms and signs of an acute breast abscess, by prolonged penicillin therapy, can be masked to such an extent that the condition may be difficult to differentiate from a lactation carcinoma.

Cases 3 and 4 illustrate well how an abscess can be so attenuated by antibiotics that the need for early incision is not appreciated and an undue amount of disability results. Perhaps it might be said that all that these last two case histories make evident is a lamentable lack of judgment in timing a surgical excision. This I freely admit, but claim in extenuation that the giving of antibiotics so relieved symptoms, and so modified the local tissue reaction, that the necessity for incision was less evident. Further, I claim to be not alone in making these mistakes.

Lake (1952) makes it quite clear that there is a growing awareness of the dangers and drawbacks of the indiscriminate use of the antibiotics. My experience in the casualty department of a large general hospital has certainly made me acutely aware of their obvious limitations. Used early and vigorously, they undoubtedly abort completely what were previously the most severe and disabling infections; one can confidently expect prompt resolution with complete restoration of function. When, however, their administration is not begun until the infection is firmly established, complete resolution unaided is most unlikely. Gratifying as may be the alleviation of symptoms and the abatement of the toxaemia, timely surgical incision to drain what may be only a small collection of sterile pus is no less necessary than it was in earlier days. Antibiotics in many instances render surgical intervention no less necessary, though they may greatly modify its extent. The relief of pain which their use affords makes it only too easy to defer a necessary incision until long after the proper time. Meantime there develops a dense local inflammatory reaction which, when operation is ultimately undertaken, bleeds alarmingly, and which interferes considerably with the establishment of free drainage.

Perseverance with the administration of antibiotics long after they have ceased to have any value is a malpractice which is in no way confined to the management of acute mammary infections. The same mistakes are made in infections at other sites, but more evidently in situations like the finger pulp or the parotid, where the clinical sign of fluctuation is in any event long delayed.

My experience suggests that their abuse presents, in the case of breast infections, a problem peculiar to this situation—namely, the development of a hard, painless, fixed mass which in its clinical features mimics very closely a lactation carcinoma. This problem in diagnosis is especially seen when the patient first presents for treatment at hospital, having been previously under the care of her own practitioner. This point has recently been briefly alluded to by Stammers (1953).

It may well be that the unsatisfactory treatment of some of these infections can be attributed to the presence of resistant organisms. This is undoubtedly all too often the case in mammary abscess, especially if the patient is confined in hospital, where by a process of selection a permanent reservoir of resistant strains seems to be maintained. This was true of one of the above cases.

Heavy dosage with, say, pencillin will in the case of a light infection lead to clinical improvement so long as the local production of penicillinase does not build up to an effective level.

Stammers has suggested that in the presence of antibiotics the character of the local inflammatory reaction is greatly modified. There may, however, be a simple explanation. On the one hand, we have an infection with prompt antibiotic treatment which clears up quickly and completely. At the other end of the scale we have the old-fashioned abscess of the pre-antibiotic days, a large collection, representing a considerable loss of tissue. Somewhere in between, when the forces of invasion and those of repair are closely matched, it seems reasonable to assume that there may develop a hard inflammatory mass surrounding a small collection of pus such as was encountered in the breast cases decribed above.

Summary

The management of four cases of acute mammary abscess is reported. Treatment was primarily with penicillin, one case receiving in addition a seven-day course of chloramphenicol.

It was observed that the classical signs and symptoms of acute inflammation were considerably altered by the use of antibiotics.

A dense hard mass of fibrous and granulation tissue surrounding a loculus of pus was a feature of all the cases. The vascularity of the mass presented a real danger when it was explored surgically, in the form of torrential haemorrhage (as illustrated by Case 2). The undue delay of operative drainage because of the masking of symptoms and signs led in turn to a long and tedious recovery.

The lessons that might be learnt from these observations are : (1) Antibiotics, though of immense value in the treatment of acute infection, especially the localization of the disease in the breast, have their limitations. (2) The treatment of a localized collection of pus is still by surgical drainage, the timing of which is now as important as ever.

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REFERENCES

Lake, N. C. (1952). *British Medical Journal*, 2, 1307.
Stammers, F. A. R. (1953). Ibid., 1, 272.

PROSTHETIC MUCOSAL HYPERTROPHY IN THE MOUTH, SIMULATING MALIGNANCY

BY

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Now that a realization of the importance of early diagnosis and treatment of cancer is spreading, not only in the medical profession but among the lay public, it is more than ever necessary to separate those benign lesions that mimic malignancy. This paper seeks to focus attention on one type that is common enough to merit detailed discussion—the mucosal hypertrophy due to chronic irritation by dental prostheses. Experience both at a large centre dealing primarily with cancer and at a general hospital dental department shows that this lesion is a regular cause of suspicion and alarm among patients, their general practitioners, general surgeons, and dental surgeons. Descriptions of the lesion are hard to find outside the dental literature. The only account that I can trace in recent general medical literature is by Simmons (1941). More recently, recognition seems to be increasing among dental surgeons. With the relative increase of the older age groups, and the increased number of dentures supplied under the National Health Service, many more of these lesions are to be expected in the future.

Clinical Picture

There are two principal sites : (1) the alveolo-buccal sulcus, immediately adjacent to the alveolus, more commonly lower than upper ; and (2) the hard palate, more or less centrally grouped round the midline.

First Type (Alveolo-buccal).—The typical lesion is a projecting elongated fleshy mass or tag on the mucosal surface adjoining the outer side of the edentulous alveolar margin (Figs. 1 and 2). Its length, parallel with the alveolus, ranges from a few millimetres to several centimetres, and its width up to about 1.5 cm. Its surface is ridged, with one or more deep furrows, and if the patient inserts his denture the edge can be seen to lie accurately in, or slip easily into, a furrow. The alveolus is atrophic and the denture fits very loosely ; usually it will be found to be an old one, commonly dating back ten years or more. The mass is fairly soft in the early stages, becoming harder with age and fibrotic changes, but there is not the spreading induration at the base that characterizes malignancy. There may be ulcerations of the furrow with a little bleeding ; inflammation may cause tenderness and increased induration at the base, which can arouse suspicion of malignancy. The patient may complain of a little lump which has inconvenienced or alarmed him, or of intermittent pain due to sepsis. In some cases the lesions are not noticed by the patient at all, but are discovered by the dental surgeon when the patient attends for new dentures. Histologically there is considerable acanthosis and thickening of the surface epithelium but no evidence of invasion ; there may be increased fibrous tissue secondary to inflammatory changes.

Second Type (Palatal).—Here the presenting lesion is on the hard palate, in the form of one or more flat or pedunculated papillomatous patches, typically a few millimetres across. There may be a complete ring of separate or fused patches, corresponding with the relief chamber or suction ring on the upper denture. The surface of the denture may be roughened and irregular. Ulceration and bleeding are uncommon. The patches may also appear at the posterior end of the hard palate, on a transverse line due to the " food line " at the back of the denture.

Case Material

The clinical material over the last eight years at the Sheffield National Centre for Radiotherapy has been reviewed. Twenty cases were found ; 10 of these were of the first type, 8 of the second, and 2 were in atypical sites, and not definitely of similar nature. (These numbers are small in comparison with the material in a dental department ; for example, at the Sheffield Royal Hospital 24 cases were seen in the dental department in a single year (1951) and approximately the same number were seen in the facio-maxillary surgical unit.)

Alveolo-buccal Cases.—Of the 10 cases in this group nine were in females. The lower jaw was the site in all but two. This preponderance in females and the lower jaw was also found by Simmons (1941). Ages ranged from 37 to 78, the mean being 51 years. The length of history varied between three weeks and three years, usually two to four months. Most lesions were 1–3 cm. long ; one unusual case showed hypertrophy extending symmetrically along nearly the whole length of the lower alveolus on both sides. The age of the denture was not routinely recorded in all cases, but was typically at least several years, the oldest set being 16 years.

Palatal Cases.—In the eight cases the sex distribution was equal. Ages ranged from 39 to 75, the mean being 63 years. The length of history ranged from a few weeks to a few months. None of the individual lesions was larger than 1 cm.

Atypical Cases.—The first case was a proliferative papilloma, 2 cm. across, on the floor of the mouth just behind the alveolus. The other was a hypertrophic patch at the posterior end of the lateral border of the tongue, apparently an enlarged papilla.

Treatment

The only danger these lesions are likely to cause arises from a mistaken diagnosis of cancer leading to radical

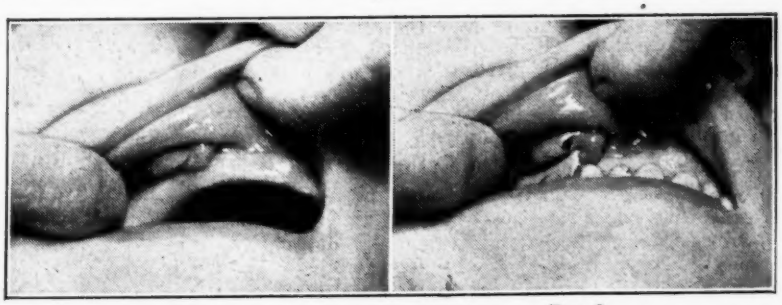

FIG. 1 FIG. 2

FIG. 1.—A typical hypertrophic mucosal lesion on the upper alveolus. FIG. 2.—The lesion in Fig. 1 in relation to the denture.

treatment by surgery or irradiation. Simmons (1941) mentions such a case treated by implanted radium to full carcinoma-lethal dosage; the tumour itself proved completely resistant to the radiation, but there was some troublesome necrosis in surrounding normal tissue. If the possibility is borne in mind, these cases are not likely to cause real difficulty, but experience suggests that this clinical entity is not widely recognized.

The important part of the treatment clearly rests with the dental practitioner, to whom the patient should be referred. If the denture is left off, and the source of the irritation thus removed, there will usually be some improvement, with disappearance of inflammation and reduction in size of the mass, especially in recent cases. Occasionally the mass may almost completely disappear; this applies particularly to small papillomatous patches on the palate. However, it will almost always be advisable to replace the denture by a completely new model. Simple trimming or adjustment may prevent contact with the mass and remove the symptoms, but the fundamental defect—that is, the unbalanced occlusion—will remain.

How should the offending nodule itself be treated? Simmons (1941) advised excision of the ridges with the diathermy loop and coagulation of the base with the diathermy button, after which healing took place in about a month. Excision, of course, provides the speediest means of removal, and is usually to be advised, especially in the alveolar cases. The later history of the present series was as follows.

Alveolo-buccal Cases.—In all cases the patient was advised to discontinue the wearing of the denture and to visit the dentist as soon as possible. In five cases the nodules were excised by the dental surgeon, either at once or after two to three months; one was removed after eight months—this was the case mentioned above with the extensive hypertrophy all the way along the lower alveolar edge. In the other five cases no removal was carried out after the denture had been adjusted or replaced (or simply left off). The nodule regressed spontaneously, till in the course of two to six months it had either disappeared or been reduced to a tiny tag giving no trouble.

Palatal Cases.—Conservative treatment was the rule here. One nodule was removed for biopsy and the base carbolized. The other seven were left alone and the denture attended to; all seven more or less disappeared in one to five months.

Atypical Cases.—The papillomatous mass behind the lower alveolus was excised, as it was comparatively large (2 cm.). The hypertrophic patch on the back of the tongue was left alone, after reassurance of the patient; it did not change, but no active treatment was necessary and the patient was discharged after six weeks.

Discussion

This hypertrophic reaction to continued trauma is now mentioned and even illustrated in standard textbooks for dental practitioners (Thoma, 1941; Stones, 1951). The former calls it "areolar hyperplasia." However, it continues to arouse special interest, as evidenced by descriptions of individual cases in dental literature (Vandory, 1937; Clark, 1947; Holland, 1949). Histological examination shows no evidence of malignancy, but there is proliferation of epithelium and reactive overgrowth of granulation and connective tissue that can resemble a fibroma. Campbell (1944) describes a case that showed masses of epithelioid cells, giant cells, and dense fibrous tissue with many lymphocytes, the whole picture suggesting a sarcoid.

Guardo (1945) calls the lesions "paraprosthetic," and distinguishes two types—acute and chronic. The acute form heals as soon as the irritant is removed; the chronic type stops growing if the cause is removed, though excision is needed before function is restored. He mentions the possibility of malignant change, but quotes no specific instances of this; no other author among those I have been able to trace mentions this important change as actually occurring, and one would like to have further details before accepting it. As an agent of cancerphobia, the potency of the lesion is attested by Hecht (1939) and Holland (1949); our own experience and that of any radiotherapeutic or dental centre amply underline this danger. One general practitioner was distressed (perhaps justifiably) by my not considering it necessary to take a biopsy but contenting myself with reassurance of the patient and his doctor.

Runnerstrom (1940) emphasizes the importance of servicing dentures after fitting; after dental extractions there is physiological resorption and atrophy of the alveolar process, and most sets of old dentures will be found to have incorrect relation to the jaw, with unbalanced occlusion; the lesions therefore are due primarily to lack of service, with a combination of mechanical trauma and bacterial infection.

In treatment most authors naturally favour simple surgical removal. This is certainly the best treatment for the great majority of cases, in which irreversible change with fibrous overgrowth has taken place. The present series, with appreciable spontaneous improvement in half of the alveolar cases and practically all of the palatal cases, shows that conservative treatment may sometimes be useful, if only as a preliminary measure. Even if disappearance is not complete, it may occasionally be enough for practical purposes; in any case, whatever shrinkage does occur will minimize the extent of surgery required. Active measures seem to be unnecessary in the case of small flat patches on the hard palate, as shown by the spontaneous satisfactory resolution in seven of the present eight cases. Anything larger would need active removal; advanced palatal papillomatosis and hyperplasia have recently been described by Thoma (1952) and Fisher and Rashid (1952).

Hecht (1939) is emphatic about the necessity for surgery; if the tissue returns to normal after leaving off the denture there may be a scar, which may interfere with the proper fit of a denture. He advises, for the palatal papillomatous hyperplasia, radical excision through the periosteum: this would undoubtedly be effective, but in the light of the present series seems unnecessarily drastic as a routine. In some alveolar cases, especially those in which the margin is extensively involved on both sides of the midline, it may be necessary to carry out the operation of "buccal inlay" after excision of the hypertrophic tissue, in order to leave a sulcus deep enough to give a denture adequate seating; a skin graft is inserted in the hollow outside the mandible, bridging the gap between the alveolar and buccal mucosae and folding to form a deep enough groove.

In general, therefore, surgical removal may be said to be the treatment of choice, with occasional exceptions, notably in small patches on the hard palate. In all cases the denture must be overhauled, and nearly always will need replacement; simple easing or trimming may relieve irritation for a time, but leaves the root cause—that is, malocclusion—untreated.

Summary

Attention is drawn to the hypertrophic tumours in the mouth due to irritation by badly fitting dentures. The commonest sites are the alveolo-buccal sulcus of upper and lower jaw and the hard palate. They are apt to be mistaken for malignant tumours. Treatment is usually by simple excision; spontaneous resolution may be adequate in the occasional case, especially for small lesions on the hard palate. A completely new denture is nearly always necessary.

I am much indebted to Mr. R. Rastall, senior hospital dental officer, Royal Hospital, Sheffield, for invaluable discussion and advice as well as for the illustrations; also to Mr. J. J. Hodson, lecturer in dental pathology, University of Sheffield, for some recent references.

REFERENCES

Campbell, J. (1944). *Brit. dent. J.*, 77, 159.
Clark, H. B. (1947). *J. oral Surg.*, 5, 348.
Fisher, A. K., and Rashid, P. J. (1952). *Oral Surg.*, 5, 191.
Guardo, R. C. (1945). *Dent. Dig.*, 51, 635.
Hecht, S. S. (1939). *Amer. J. Orthodont.*, 25, 574.
Holland, D. J. (1949). *J. oral Surg.*, 7, 75.
Runnerstrom, G. (1940). *Northw. Univ. dent. Res. Bull.*, 40, 15.
Simmons, H. T. (1941). *British Medical Journal.*, 1, 119.
Stones, H. H. (1951). *Oral and Dental Diseases*, 2nd ed. Livingstone, Edinburgh.
Thoma, K. H. (1941). *Oral Pathology*. Kimpton, London.
—— (1952). *Oral Surg.*, 5, 214.
Vandory, W. (1937). *Z. Stomatol.*, 35, 1184.

SIMPLE DEPRESSED FRACTURE OF THE SKULL

BY

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Whether or not to advise elevation of a simple depressed fracture of the skull which is symptomless is a recurring, albeit an infrequent, problem. Most depressed fractures are compound, and the indication for operation in these cases is absolute.

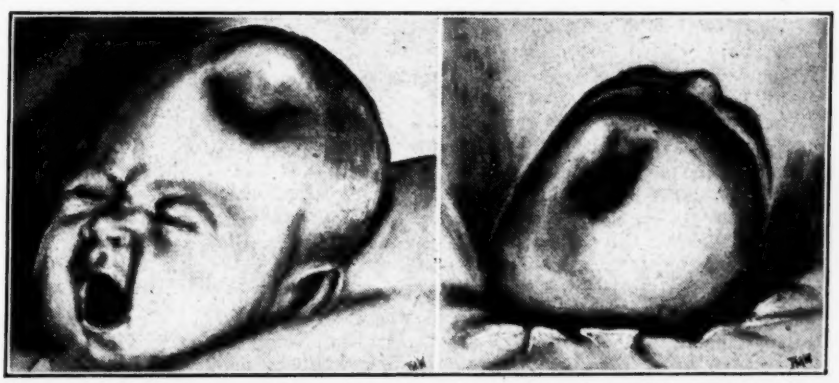
When a child is seen with a slight depression, an unbroken scalp, and a complete absence of symptoms, there may be a natural inclination on the part of the medical adviser and the patient's relatives to leave well, or what is apparently well, alone. *X*-ray films may merely confirm the depression and the electroencephalogram may be normal, but nevertheless a piece of the inner or vitreous table of the skull may have been driven through the dura mater into the brain. This is illustrated in the following case.

Case 1.—A boy aged 9 fell from a swing and dented his left parietal region. He was unconscious for about 20 minutes and then recovered completely and walked home. When seen at the Cardiff Royal Infirmary some five months later he had no symptoms and presented no abnormal features except a shallow depression in the left parietal region which was confirmed by *x*-ray examination. The nervous system was normal, as was also the electroencephalogram. At operation an in-driven fragment of the inner table of the skull was found to have penetrated both dura and brain, and to have anchored the brain at the site. A flap of bone, including the depression, was removed, reversed, and replaced after cutting away the projecting bony fragment which had entered the brain, and after smoothing the rather uneven surface of the inner table, which was now lying outwards. The boy made a good recovery, and it was concluded that freeing the anchored and developing brain was desirable in order to avoid possible complications in the future.

Depression in the Newborn Child

At birth and in infancy the skull bones are so soft that in these cases there is indentation without fracture, but it is convenient to regard them in the same category, as they are examples of traumatic depressions nevertheless.

Case 2.—A male baby delivered by forceps had a deep indentation in the left fronto-parietal region. He appeared in all other respects normal, and was seen at intervals until 2 months old; but as during this time there was no indication of the restoration of the normal contour of the skull by the disappearance of the indentation, this was effected by operation, with a satisfactory result. After turning down the scalp, a flap of bone was cut with scissors and with the thumbs the depression was pushed out and the osteoplastic flap replaced. The baby thrived and now has a skull of normal appearance, and what was a considerable reduction in intracranial capacity due to the deep indentation has been restored to normal.



Drawing of baby boy aged 2 months with persistent depression in left frontal region (Case 2).

Diagnosis of a Simple Depressed Fracture

A depressed fracture is usually obvious, but is not always so, especially if lying beneath the temporal muscle and its overlying fascia. In these circumstances *x*-ray examination in strictly antero-posterior as well as lateral planes may also fail to detect the depression. Films taken after slight rotation of the skull will make it obvious, however, as in the following case.

Case 3.—A naval stoker aged 26 fell from a plank on to the quayside at Cardiff docks and lost consciousness, which he regained in an ambulance on the way to hospital. He developed a swelling over the right side of the forehead, on which there were some abrasions, and the left eye showed subconjunctival haemorrhage. No depression could be felt, but slightly rotated antero-posterior views of the skull showed a depressed fracture underneath the left temporal muscle. Six days after his admission to hospital the depressed part of the left squamous temporal bone was elevated after first reflecting the temporal muscle. Recovery was uninterrupted.

Any error in diagnosis is usually in the opposite direction, of suspecting a depressed fracture when none exists, and what is felt and thought to be a depressed fracture is in reality a haematoma with a soft centre and firmer periphery.

Operative Treatment

If a depressed fracture is compound the question of whether to operate or not does not arise. Operation is indicated, as it is in the case of compound fractures occurring elsewhere in the body, and for a similar reason. It is suggested that simple depressed fractures should likewise be operated upon. Two points in technique may be referred to. (1) It is advisable to operate early, before union has taken place. In this early phase the bony fragments can be elevated, but after union has occurred this is no longer possible. To try to lift up the depression, which is really a reversed bridge, is like applying pressure to the arch of a cantilever bridge, and is quite futile. In this phase a block of skull comprising the fracture should be removed, reversed, and replaced. (2) The best way to deal with the indented skull of the infant is to cut out a flap of bone with a pair of scissors, reflect it on its base as a hinge, press up the depressed area with the thumbs, and replace the flap.

Conclusions

Further cases might be quoted, but these serve to illustrate that simple depressed fractures should be elevated to restore the contour and capacity of the skull and to free what may be an anchored brain in the hope of avoiding future complications such as epileptic attacks. Early operation is advisable; not urgently as in compound fractures, but at a time convenient to patient and surgeon. Secondly, in the case of fractures in the temporal region, depression should be suspected and special *x*-ray examination made to ascertain whether it is present and masked by the temporal muscle and a tense overlying temporal fascia. Lastly, deep depressions in the skulls of the newly born should be pressed out within a few months of birth, if during this time no tendency is observed for natural restoration to take place.

I am indebted to Miss J. M. Williams, of the Welsh National School of Medicine, for the drawings.

TEEPOL IN THE PREPARATION OF SPUTUM FOR TUBERCLE CULTURE

BY

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AND

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Demonstration of tubercle bacilli in sputum is necessary for diagnosis and for controlling risks to contacts, and is also, owing to recent developments in chemotherapy, of increasing importance in assessing treatment. Thus identification of this organism constitutes a growing duty of public health laboratories.

Pottenger (1930–1) showed that microscopical examination of a Ziehl–Neelsen film for 10 minutes will reveal less than 88% of positive specimens. The value of selecting a purulent portion of sputum for preparing films has been re-emphasized by Spendlove *et al.* (1949), who clearly demonstrated the superiority of this procedure as compared with concentration by alkali treatment and centrifugation, which seems to reduce the acid-fast properties of the organism. Corper (1928) stated that over 100,000 tubercle bacilli must be present per millilitre of sputum before they can be detected microscopically in a fairly thick film, while accord- to Cruickshank (1952) the number is from 10,000 to 50,000. Thus adequate direct examination of sputum films is time-consuming, and even when thoroughly carried out some 10% of positive specimens probably escape detection. Culture methods also have their defects, and some microscopically positive sputa fail to yield growths. Cruickshank noted as high as 27% failures with weakly positive sputa in general, and 68% when chemotherapeutic agents had been administered. However, it is clear from the work of Dubos (1946) that the tubercle bacillus is fickle in its reaction to artificial nutrient environments.

Direct examination and culture are complementary, and should be carried out in parallel in order to minimize false-negative results. This is all the more important since the valuable method of guinea-pig inoculation can be performed only on a limited scale and also has its failures. Recently the Public Health Laboratory Service Working Party on the Diagnosis of Tuberculosis (Report, 1952) described very thorough experiments to determine which of four techniques for homogenization and culture of sputum yielded the greatest proportion of positives, and concluded that "sodium hydroxide proved significantly better than any other methods." We have obtained promising results by a different method which is exceedingly simple and rapid as compared with the alkali technique.

Method

The detergent "teepol," stated by the manufacturers to be a solution of sodium higher alkyl sulphates, was used to homogenize the specimen and kill contaminants. Trial sputa, mainly from sanatorium patients and received after one to three days in transit, consisted of 3–10-ml. specimens in 1-oz. screw-cap universal containers with "blackol" liners. First a direct smear was stained Ziehl–Neelsen and examined for five minutes by each of two people. The number of tubercle bacilli found in positive films during the 10-minute search varied from abundant to only one or two. To each specimen was than added an equal volume of teepol, the mixture being shaken once or twice for a few seconds and kept at room temperature for six hours in the case of a third of the specimens, the others being left for 24 hours. The result was a homogeneous and syrupy mixture. The whole surface of a slope of Löwenstein–Jensen medium in a universal container was inoculated with three small (2-mm.) loopfuls of each mixture and kept at 37° C. for six weeks.

Results

Of 142 specimens, 41 were positive microscopically, and growths of tubercle bacilli were obtained from all but one of the latter. Of the 101 microscopical negatives, eight proved positive on culture, two of which were examined for virulence and found to be virulent to the guinea-pig. Three further specimens, microscopically a positive and two negatives, were discarded because of contamination. Growth was usually observed in the third or fourth week.

It is not yet known whether the shorter exposure will yield a larger proportion of positive results, or whether the carry-over of a small amount of detergent benefits the culture, but apparently it is not harmful. The effect of larger inocula has yet to be tried. A 50% watery dilution of teepol often fails to homogenize and so to sterilize even in 48 hours, coliform organisms and yeasts mainly surviving. The method is apparently applicable to other types of specimen, urines having been successfully cultured.

REFERENCES

Corper, H. J. (1928). *J. Amer. med. Ass.*, **91**, 371.
Cruickshank, D. B., Sellors, T. H., and Livingstone, J. L. (1952). *Modern Practice in Tuberculosis*. Butterworth, London.
Dubos, R. J., and Davis, B. D. (1946). *J. exp. Med.*, **83**, 409.
Pottenger, J. E. (1930-1). *J. Lab. clin. Med.*, **16**, 985.
Report (1952). *Monthly Bull. Minist. Hlth, Lond.*, **11**, 187.
Spendlove, G. A., Cummings, M., and Patnode, R. A. (1949). *Pub. Hlth Rep., Wash.*, **64**, 574.

The seventh annual report of the Institute of Child Health (University of London) includes an account of research undertaken or projected at the Institute during 1952. In January a full-time physiologist was appointed and is at present engaged on investigations of renal function. The Institute has undertaken supervision of the Population Investigation Committee's survey of growth and development being carried out by Dr. J. W. B. Douglas. At the Child Study centre the investigation into normal growth and development is proceeding, and the report of the results of the pilot survey was produced during the summer. Improved techniques of measurement have been introduced; *x* rays have been used to determine tissue depth, and an accurate method for assessing this has been determined. Dr. A. P. Norman has continued his clinical investigations of fibrocystic disease of the pancreas and (with Dr. L. I. Wolff) of hepatic and renal function in full-term and premature neonates. Dr. J. Dean and Mr. D. I. Williams have continued their work on nocturnal enuresis.

Medical Memorandum

Congenital Tracheo-oesophageal Fistula Without Oesophageal Atresia—With Resultant Asphyxial Death

Congenital tracheo-oesophageal fistula in the presence of a normal oesophagus is an extremely rare occurrence. The literature contains only isolated reports of this condition : two cases are described in which correction had been attempted (Imperatori, 1939 ; Haight, 1948). Haight reports having observed this anomaly in two out of a series of 65 cases of oesophageal anomalies.

CASE REPORT

An African woman aged 38 was brought to the Government mortuary. She had been found in a kitchen apparently dying, and soon afterwards, at hospital on October 27, 1950, was certified as dead.

At necropsy she was found to be well developed ; weight 145 lb. (65.8 kg.); height 64 in. (163 cm.). There were bright-red bilateral subconjunctival haemorrhages and subaponeurotic petechial haemorrhages over the frontal region of the scalp. The brain was congested and oedematous, and there was coning of the medulla. The heart muscle was flabby and friable ; otherwise the heart was normal. The blood was very dark and fluid. Ruptured air vesicles were found along the surfaces of the lungs, which were slightly ballooned, congested, and oedematous, with mucopus in some bronchioles. Midway down the oesophagus, and in the posterior wall, there was an old fistulous communication with the trachea, measuring 1¼ by ¼ in. (4.4 by 1.9 cm.). The edges of this fistula were well rounded and firm. Lodged in the trachea, between this fistulous opening and the hypopharynx, was a single bolus of meat (see illustration). Curling of the epiglottis was noted. The liver, spleen, kidneys, and gastric mucosa were congested. The stomach contained a partly digested meal. The rest of the bowel was normal.

Photograph of specimen. Note the fistula in the otherwise normal oesophagus; also note the lower end of the bolus of meat showing in the upper part of the fistula while still impacted in the trachea.

A histological report on the lung read as follows : "Section of this lung shows that it is congested, with patchy extravasation of red blood cells and oedema fluid into the alveoli. In one of the small bronchioles there is an acute inflammatory exudate. The lymphoid foci in the lung substance are hyperplastic, with plasma-cell infiltration. The histological features suggest an early bronchiolitis." Histological examination of the edge of the fistula showed no evidence of any pathological condition in the tissues. The cause of death was asphyxia due to impaction in the trachea of a regurgitated bolus of meat through a congenital tracheo-oesophageal fistula.

The C.I.D. subsequently obtained the following history of the deceased up to the time of death: "Deceased had been employed for the past four years in domestic service by a Chinese woman in the City of Johannesburg. During this time she was periodically indisposed, and was treated at hospital ; the nature of her complaint was not known, but it appeared that she was receiving injections in her breast, since she once reported to her employer that she intended discontinuing her hospital visits because the breast injections were too painful. On the night she died she was found by her employer lying on the kitchen floor 'shivering and with her tongue darting in and out of her mouth'; she was unable to speak. That evening she had been given soup-meat for supper. She was a small eater. She had always complained of pain in her chest."

Despite all efforts by the police no evidence of previous hospital treatment could be found. Such evidence at the best of times is extremely difficult to trace, let alone in the case of a deceased person.

DISCUSSION

The rarity of congenital tracheo-oesophageal fistula without other abnormalities of the oesophagus is substantiated by a review of the literature (Haight, 1948). The symptoms consist of choking and coughing coincident with the ingestion of food and particularly liquids. Leven and Lannin (1945) remark that because of difficulties in establishing the diagnosis the condition may continue to remain unrecognized and untreated, giving the impression of being an acute recurring pneumonitis. Also in patients who have survived more than a few days a recurring pneumonitis has been the reason for frequent admissions to hospital.

In the above case the initial appearances—namely, subconjunctival haemorrhages, subaponeurotic haemorrhages, cerebral congestion and oedema, colour and fluidity of the blood, ruptured air vesicles, and ballooning of lungs—all suggested an asphyxial death, and a very rapid one. Loubser (1945) states that when the process of asphyxiation is very sudden and complete, especially in those cases due to obstruction by foreign bodies, death takes place rapidly, with marked signs of asphyxia, and especially small subconjunctival or subaponeurotic haemorrhages.

The sequence of events suggested is that this woman was attempting to swallow a large bolus of gristly soup-meat (which aptly describes the impacted bolus), or that, owing to some sudden disturbance, she involuntarily swallowed the bolus, which passed partly down the oesophagus ; and then, because of some vagal inhibition, spasm with regurgitation occurred, the bolus shooting upwards and backwards through the fistula and into the trachea and lodging there, with resultant complete obstruction and rapid asphyxia.

The question that immediately arises is, How did this woman live for so long with so large an asphyxial potential ? The histopathology suggests that minute fragments of foreign material were inspired via the oesophagus through the fistula and via the trachea into the lungs, with resultant inflammatory foci. This would also explain her story of ill-defined chest pains for which she received hospital treatment over a number of years. Professor R. H. Mackintosh, medico-legal pathologist to the Union Government, suggested that a major catastrophe was prevented all these years because of purely mechanical reasons—namely, involuntary contraction of the oesophagus and trachea with swallowing, resulting in almost complete closure of the fistula as food or liquid passed down the oesophagus. This must be the accepted view.

I am indebted to Professor R. H. Mackintosh for permission to publish this case and also for helpful discussion. My thanks are also due to Sergeant D. J. van Schalkwyk, Assistant Curator, Government Mortuary, for photographing the specimen.

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REFERENCES

Haight, C. (1948). *J. thorac. Surg.*, **17**, 600.
Imperatori, C. J. (1939). *Arch. Otolaryng.*, **30**, 352.
Leven, N. L., and Lannin, B. G. (1945). *J. Lancet*, **65**, 179.
Loubser, C. J. N. (1945). "Asphyxia—Its Medico-legal Aspect in South Africa." M.D. thesis, University of Witwatersrand.

Arrangements for priority and special rations for invalids are set out in a new edition of a Ministry of Food Memorandum, Med. 2 (1953). The Food Rationing (Special Diets) Advisory Committee of the Medical Research Council has recommended two changes in this edition. Patients suffering from an organic disorder affecting swallowing are to be granted an extra ration of fats in addition to the extra sugar which they are allowed at present, and the extra ration of fats and meat given to children with coeliac disease on a gluten-free diet has been extended to cover all adult cases of tropical sprue and steatorrhoea. The Memorandum is being distributed to all registered medical practitioners in the United Kingdom.

Reviews

FOUNDATIONS OF MODERN PHARMACOLOGY

Adventures in Physiology, with Excursions into Autopharmacology. A selection from the scientific publications of Sir Henry Hallett Dale, O.M., G.B.E., F.R.S., M.D., F.R.C.P. With an introduction and recent comments by the author. (Pp. 652, with many figures. £6 6s.) London: Pergamon Press. 1953.

There are thirty papers and lectures in this book, chosen for continuity of interest; they are mainly on humoral transmission and histamine. One might wonder at first, as the author says he did, whether it was worth while reprinting papers which were readily accessible—and, what the author did not say, papers which are already part of contemporary knowledge and regularly consulted by physiologists and pharmacologists the world over. The answer is that we have here, in collected and convenient form, a series of papers that have played a large part in the foundation of modern pharmacology, and indeed have made history. Moreover, the author has now added some valuable comments, or second thoughts, bringing the papers under the light of more recent knowledge. It is these comments which provide the really fascinating part of the book. They show that the author has not only continued to read widely, but has adjusted his earlier views to modern conceptions. Often, in preface and in comments, he refers to instances "in which accident seems to have favoured, or even to have prompted, some scientific enterprise of mine." And indeed, if we are to believe the author, not even the Three Princes of Serendip were more fortunate in their serendipity than he. One can only agree with him up to a point: in the extract above quoted the operative word is "enterprise." The crucial accident was that the author happened to be endowed with the genius and the enterprise to follow up the unexpected events which happen from time to time no doubt, though so often with no further consequences, to all of us.

Yet in spite of this good fortune, as he calls it, that eternal spirit of discontent which is part of the equipment of the scientific mind shows through at times. What he seems to regret is not having been endowed with precognition: "Doubtless I ought to have seen that *nor*-adrenaline might be the main transmitter" (in 1910); and, "Even more curious, however, is the fact that, by this time (1914), both Elliott and I seem to have become shy of any open allusion to the 'chemical transmission' theory, which he had originated ten years earlier." The title of the book is an apt one, for few research workers can look back on their earlier work with the same satisfaction, and with such searching self-analysis, and see that in retrospect it was more adventurous than appeared at the time. No better book could be studied by the young research worker needing stimulus and encouragement. There is a bibliography of 253 papers and lectures by the author.

The work has been well printed, and the illustrations have come out well; the opportunity has been taken for the correction of some misprints in the originals, not, however, without introducing some others—for example, in title No. 11, p. 26, where "retraction" should read "retractor."

C. LOVATT EVANS.

INFECTIOUS MONONUCLEOSIS

Infectious Mononucleosis. By Sidney Leibowitz, M.D. Modern Medical Monographs 5. (Pp. 164. $4.75.) New York: Grune and Stratton. 1953.

This monograph is based on 25 cases studied in detail by the author and a review of the literature whose thoroughness is attested by a list of 377 references. It is possible to speak of various phases in the history of infectious mononucleosis: the clinical phase, in which glandular fever was recognized; the haematological phase, in which the changes in the blood picture were studied and the identity of acute mononucleosis and glandular fever was established; the serological phase associated with the Paul–Bunnell reaction; and, most recent of all, the pathological phase. Knowledge of the pathology has come partly from biopsies of the glands and the liver, but chiefly from the 38 fatalities which have accumulated over the years, some from accidents and some from the disease itself. Infectious mononucleosis is not a killing disease, and the rare deaths are usually the result of rupture of the spleen or respiratory paralysis from involvement of the central nervous system. The picture at post mortem is one of widespread perivascular lymphocytic infiltration.

Readers of this monograph will probably be impressed by the frequency of involvement of the liver, the common occurrence of abnormalities in the electrocardiogram, and the seriousness of involvement of the central nervous system. When this last occurs, there may be few of the usual clinical features of infectious mononucleosis, and the mortality is high—about 11%. Dr. Leibowitz believes that the frequency of positive serum reactions would be increased from the present 83% to 100% if the tests were adequately performed, and he is sceptical of the existence of cases with a persistently negative Paul–Bunnell reaction. There is certainly evidence of the existence of an undefined virus disease or diseases which have a clinical resemblance to glandular fever but do not show the typical haematological and serological reactions. This is a clearly written, useful, and well-produced monograph, which gives a good account of this interesting disease.

L. J. WITTS.

OBSTETRICS IN PHILADELPHIA

Clinical Obstetrics. By Members of the Staff of the Pennsylvania Hospital. Edited by Clifford B. Lull, M.D., and Robert A. Kimbrough, M.D. (Pp. 732; 392 illustrations and 8 coloured plates. £4.) Philadelphia and London: J. B. Lippincott Company. 1953.

This book is written by 20 members of the staff of the Pennsylvania Hospital with Dr. Clifford B. Lull the editor initially. Unfortunately he died in 1951, and thereafter Dr. Robert A. Kimbrough assumed the leadership of the team and dedicated the work to the memory of the first editor. By and large it is an account of the practice of the division of obstetrics and gynaecology of a hospital whose history goes back more than 200 years. It is intended primarily for the use of the hospital's own students and as an adjunct to the practical instruction which they are given. Nevertheless, it is not far short of being a complete undergraduate textbook, and omits little which any student should know. Its style, presentation, and illustration are unusually attractive, and are worthy of study by anyone with ideas of writing a book.

This sumptuous production has clearly been a labour of love by a staff devoted not only to their work but to their hospital, whose tradition and eminence they wish to see maintained. So the foreword consists of a history of the Pennsylvania Hospital, and the closing chapters are concerned with maternal and foetal results obtained in their hospital, city, and state; with an analysis of avoidable factors in the deaths; and an indication of the training, standards, and obligations of obstetricians of the present and future.

Probably few in Britain will find themselves able to buy this expensive book, whose strongest appeal is to those connected with Philadelphia. Nevertheless the idea behind it and the excellence of its execution might well be copied by some of the older and larger teaching institutions here, those whose tradition for service, scholarship, and research deserves handing on to the new generation.

T. N. A. JEFFCOATE.

PATIENTS' ART

Experimental Studies in Psychiatric Art. By E. Cunningham Dax, M.B., D.P.M. Foreword by Sir Steuart Wilson. (Pp. 100; 51 illustrations. 18s.) London: Faber and Faber. 1953.

The earliest form of human communication known to us was in drawing and painting. The cave artists painted because they liked painting and not because they were sick. It gave expression to their creative imagination.

Dr. Dax, aware that the arts had been used extensively in mental hospitals, set himself the almost impossible task of organizing the output of the creative activity of the mind under standard conditions. Thus might we use the arts scientifically in psychological medicine. Scientific assessment of this work would, he believed, enhance its diagnostic and therapeutic value. This applied also to the playing of selected music to patients. He attempted experimentally to correlate the effects of music with the production of paintings. A record was played to the patients, and then followed nine and a half minutes of painting. These results were thought to be "statistically significant." Individual experiments were a failure because spontaneity was lost in the process, while group products were awkward material for evaluation and the results inconclusive.

Far and away the most important part of this interesting and original book is Dax's description of the facilities for art work at Netherne Hospital. He had an enthusiastic and invaluable collaborator in Mr. E. J. Adamson, who was in charge of the groups engaged in painting and drawing. He showed genius in establishing the right atmosphere in which the creative imagination of the patients could easily find expression. Mr. Dax is unnecessarily apologetic about the lack of scientific validation in the artistic productions of his patients. The invisible and unrecordable accompaniments which to the artist and others *are* the picture cannot be measured. The "art therapy" enthusiasts (and the doubters) will find this book well worth reading. They need not worry when they cannot *prove* the value of the painting.

E. A. BENNET.

BIBLIOGRAPHER'S DELIGHT

Jacob de Castro Sarmento. By Dr. Augusto d'Esaguy. (Pp. 119. No price.) Lisbon: Edicoes Atica.

Jacob de Castro Sarmento (1691–1760), an able and versatile physician of scientific tastes, practised very successfully in London during most of his active life. His career provides enough puzzles for the most ardent bibliographer, for his name appears in several forms and with several initials. He wrote in six languages, and all his works are rare and some very rare indeed. It has even been suggested that there were two or more men of the same or similar names.

Sarmento was born at Braganza of Jewish parents who practised secretly the rites of their religion. Jews had been expelled from Spain in 1492. The Inquisition took longer to enter Portugal, where it never obtained the same hold. In that small country a certain number of Jews did succeed in maintaining an underground existence until able to declare themselves in quite modern times. Sarmento at any rate gained some slight knowledge of Hebrew. He studied at the Universities of Evora and Coïmbra and practised at Lisbon. In 1720 he came to London. There he attached himself to the synagogue of the Spanish and Portuguese Jews, acting as the physician to its members.

In London Sarmento was one of the very earliest to advocate the practice of "variolation." This had been very recently introduced from the East by Lady Mary Wortley Montagu. It consisted in inoculation from the pus of a mild case of smallpox and preceded Jenner's vaccination by some 60 years. Sarmento's first publication (London, 1721) was on variolation and was in Latin. In 1723 he printed a work of conventional Jewish piety which leaves no doubt that he had openly reverted to his ancestral faith. His rise in practice was rapid and was maintained. He was licensed by the College of Physicians in 1725, was elected to the Fellowship of the Royal Society in 1729 and to that of the College in 1739. He maintained a correspondence with scientific men in Portugal and Brazil, and in both countries his opinions continued to be highly esteemed. He introduced the Newtonian philosophy into his native land by his accounts of parts of Newton's works in Portuguese. He also translated into Portuguese certain works of his own contemporary, Stephen Hales, and drafted a scheme for an edition of the works of Francis Bacon. Sarmento's writings on materia medica long held the field. Late in life he left the synagogue. He had two sons, one of whom became a British general.

The writings of Sarmento were chiefly in Portuguese and are very numerous, while he himself is credited by Dr. Augusto d'Esaguy with no fewer than 28 works. His reputation was maintained by editions of his works or of works ascribed to him for nearly three-quarters of a century after his death. The late Dr. Maximiano Lemos wrote a learned book on Sarmento, but Dr. d'Esaguy has been able to add considerably to his list of Sarmento's writings, though he does not include his contributions to the *Philosophical Transactions* of the Royal Society. Dr. d'Esaguy's reproductions of the title-pages of some of the rare and less accessible works of Sarmento will be specially welcomed by bibliographers.

CHARLES SINGER.

SYPHILITIC OPTIC ATROPHY

Syphilitic Optic Atrophy. By Professor Walter L. Bruetsch. (Pp. 138; 30 illustrations. £2.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

This monograph appears at an opportune time. The development of blindness in the late stages of syphilis, coming on slowly and inexorably some 20 years after the infection had been incurred either in the congenital or acquired disease, had been recognized in a vague way for over a century and was fully established as a clinical entity in the 1880's by such writers as Fournier, Erb, and Westphal. To-day, although the incidence of the disease is much less in this country than it was a quarter of a century ago, it is still an important cause of blindness, while in the United States it has been variously estimated that there are between 25,000 and 50,000 persons blind from this cause. From time to time many theories have been advanced to explain the implication of the optic nerve, and until the revolutionary work of Lére in 1904 it was generally accepted that the main lesion lay in the ganglion cells of the retina; the atrophy was thus considered, and is usually called, "primary" optic atrophy. Pathological examinations have been relatively few, but the histological material gathered by Bruetsch fully bears out the view of the early French author that all cases of the disease have the characteristics of a secondary atrophy due to an inflammatory meningitis at the base of the brain affecting usually the intracranial portion of the optic nerve and the chiasma. It would therefore seem logical to substitute the term "syphilitic" for "primary" optic atrophy.

While the pathological material presented in this monograph is of very great value, the therapeutic corollary is of still greater importance, for the author contends, and backs up his contention with impressive material, that if diagnosed in its early stages the progress of the disease can be arrested. This is a novel view to take of a condition hitherto considered hopeless, and it depends upon the results of newer methods of therapy by malaria and penicillin. In the author's view these should replace therapy by the arsphenamines. Early diagnosis in suspected cases—a matter which depends chiefly on a close study of the peripheral visual fields—is thus of paramount importance and holds the key to the eventual elimination of a disease which hitherto has been almost uniformly associated with tragedy.

The monograph is short, easily read, beautifully illustrated, and persuasive in its argument. It will be of unusual value to the syphilologist, neurologist, and ophthalmologist as well as the general physician.

STEWART DUKE-ELDER.

The new edition of the *Medical Directory*, in its handsome red-and-gold covers, contains the usual information about members of the medical profession and medical institutions. We learn from a table that nearly a quarter of the 46,000 doctors in England live in London, and that the 8,917 doctors in Scotland are 2,000 fewer than the London doctors. Published by J. and A. Churchill, the price is 72s. (two volumes). *The British Journal Photographic Almanack 1953*, as well as containing much of interest to any doctor whose hobby is photography, includes a section specifying the suitability of many photographic materials to special subjects in medical photography. It is published by H. Greenwood, London, for 5s. (cloth bound 7s. 6d.).

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SIR HENRY DALE'S OPUS

Not often has the work of one man and his associates been so richly fruitful as that inspired and carried out by Sir Henry Dale, O.M. Publication of some of his writings in a book (reviewed at p. 1434) is a reminder of the pervasive influence his work has had on the progress of medicine in the first half of this century. It was from 1904 to 1914, when Dale was working with Laidlaw at the Wellcome Laboratories, together with Barger, Carr, and Ewins, that the outstanding work was done which determined the lines of much that followed later. If the lectures are excluded, the papers from that period occupy nearly half the book.

Few papers have been written which have maintained their importance for so long as that published in 1910 by Barger and Dale on the chemical structure and sympathomimetic action of amines. It remains even to-day the principal contribution to this subject, the importance of which for all doctors is evident when we reflect on the extensive and still-growing use of substances like ephedrine, amphetamine, and isoprenaline. Closely connected with this work was that on the specific alkaloid which Barger and Carr obtained from ergot and called ergotoxine. Dale's exhaustive study of its action revealed that it prevented many of the motor effects of adrenaline, leaving the inhibitory actions unaffected. During the last twenty-five years there have been continuous efforts to find other substances with similar properties though more suitable for clinical use. A compound which can prevent the vasoconstrictor action of adrenaline may also lessen the vascular tone maintained by the sympathetic system and so be used to lower blood pressure in hypertension ; but such a substance must not, like ergotoxine and ergotamine, itself cause vascular spasm and so be liable to cause gangrene. Almost every year recently a new substance has been introduced for this purpose, with varying success.

The development of the study of histamine, which was made together with Laidlaw and later with Richards, had important results for physiology and physiological methods, for pathology, and finally for therapeutics. The problem left unsolved by the papers written with Laidlaw in 1910 and 1911 was how to explain the fall of blood pressure which histamine caused when injected into an animal, in view of the fact that it caused vasoconstriction on perfusion through the vessels of an organ. The results published in 1918 with Richards put forward what was then a revolutionary conception. This was that the capillary bed can vary greatly in size, can constrict or expand independently of the arteries, and plays an important part in determining the level of the blood pressure. It was found to be on this capillary bed, which did not function in conditions of perfusion as carried out until that time, that histamine exerts its action in the body. But for the publication of Krogh's work almost immediately afterwards, which came to similar conclusions on capillary activity by more direct methods, Dale and Richards would have received greater recognition for their discoveries than they did. Their results were obtained by devising conditions in which the vessels of the perfused organ behaved as they behaved in the body. The perfusion methods were developed further later on, and culminated in the Dale–Schuster pump, described in 1928, which has been an invaluable tool.

For pathologists the study of histamine was important on two grounds. First, the phenomenon of histamine shock described by Dale and Laidlaw in 1919 led them to conclude that "a large group of poisonous substances of animal or bacterial origin" could increase capillary permeability and thereby cause oedema and circulatory collapse. Secondly, the study of the action of histamine was related by Dale to his work on anaphylaxis, which he showed in a most convincing manner was due to the reaction between antigen and a precipitating antibody inside the cell. He explained the similarity of the effect of histamine in certain species to anaphylaxis in that species as due to the release of histamine by the antigen-antibody reaction, and expressed his belief that allergic responses arose in the same way. Therapeutics has gained finally because it is on the basis of this work that the antihistamine compounds have been found useful in so many allergic and other conditions.

But perhaps it is for his investigations on acetylcholine that Sir Henry Dale is best known. In 1914, before Loewi had given his demonstration of the humoral transmission of vagal stimulation, Dale wrote, "One can conclude that there is some degree of biochemical similarity between the terminations of voluntary nerve fibres in striated muscle and the mechanism connected with the peripheral termination of craniosacral involuntary nerves." In his book Dale now refers us to arguments set out by T. R. Elliott (to whom the *Adventures* are dedicated) in 1905 and 1907 for regarding the motor end-plates of striated muscle fibres as homologous with autonomic ganglion cells. No matter how the credit for this remarkable

prescience should be distributed, this 1914 paper of Dale's and the papers with Gasser in 1926 and with Gaddum in 1930, form a series of imposing preludes to the final demonstration in 1936 of acetylcholine as the transmitter of impulses passing along the voluntary motor nerves, in which Brown and Feldberg and Vogt all assisted. From this work has come the use of neostigmine in myasthenia gravis and as an antagonist of D-tubocurarine in anaesthesia. The work was followed by the demonstration of humoral transmission in ganglia, and from there the path has led to the methonium compounds and the use of hexamethonium to ensure a bloodless field in surgery.

This record, truly impressive in itself, is a justification too of the need for single departments of pharmacology and biochemistry where organic chemist, biochemist, and biologist should be able to study a problem together. We may fittingly conclude by quoting from a leading article in this *Journal* on the occasion of Sir Henry Dale's election as President of the Royal Society in 1940: "His life has been spent in the service of experimental medicine, and it is a remarkable fact that his major researches in the laboratory have subsequently found important application in clinical medicine."

TEAMWORK IN GENERAL PRACTICE

As last week's *Journal* went to press during the Annual Conference of Local Medical Committees it was not possible to include a complete account of the Minister of Health's address to it. Space and time only allowed us to report and comment on Mr. Macleod's observations on the rising cost of the pharmaceutical service and measures proposed to stabilize this. Confronted by a picked audience eager to hear him speak, Mr. Macleod responded by going beyond his prepared brief and quickly established a relationship with the Conference which should have wide repercussions. Maybe he will find it possible to repeat this experiment by addressing, one day, the Representative Body. What he said was in effect a straight answer to Left-wing assertions that the present Government is out to destroy the Health Service. Mr. Macleod sees in the N.H.S. a possibility to realize more fully than before "the full conception of the family doctor." The general practitioner must be, he declared, the leader of the domiciliary health services. More patients should be treated in their homes, in their own familiar surroundings, and fewer in hospitals. This would greatly enhance the value and interest of the work of the general practitioner. He stressed the importance of direct consultation between family doctor and consultant. The general practitioner should be promptly informed when his patient leaves hospital, and when he referred a patient for consultation he should always receive a considered opinion from a senior member of the staff. The general practitioner should have direct access to *x*-ray and pathological facilities. He should be considered part of the hospital service of his area. There should be complete liaison between the general practitioner and the local health authority, particularly in preventive work. In this matter conditions varied in different parts of the country. Some feared that where many people were concerned with the welfare of the patient there was a danger of the general practitioner's being crowded out. Here Mr. Macleod emphasized once more that the general practitioner should be the clinical leader of the team. "We are engaged," he remarked, "in a great experiment in social medicine, but it must not be strangled by too much administration or too much central direction." He ended with a plea for co-operative effort between himself and his department and the professions engaged in the Service: "It is only in partnership that we are going to solve this problem and achieve the true potentiality of the National Health Service."

The Conference responded with enthusiasm to a Minister who did not hector or lecture to them, who spoke, indeed, not as a politician wishing to score debating points but as someone engaged in a different capacity in the same kind of work as others and wishing to make the best of it with them. The problems of general practice and of the general practitioner are not peculiar to this country. With local variations they are fundamentally the same in all countries able to make the fullest use of the resources of modern medicine. These resources cannot be brought to the sick person by any one practitioner working in isolation from his colleagues. Nor can they be parcelled out piecemeal by this or that expert on a conveyor-belt system. The service of the health visitor, of the physiotherapist, of the consultant and the specialist, of the clinical pathologist, must be co-ordinated and controlled by someone if the patient is finally to be treated as a whole person and not as an assembly of bits and pieces of disordered physiology. Mr. Macleod puts the general practitioner firmly in the centre of the picture as the clinical leader of the team whose various special skills are brought to bear on the diagnosis and treatment of the person whose mind or body is afflicted. And it is only the general practitioner who is in a position to relate all this to the individual circumstances of the patient as

a member of a family and to his work. Integration and co-ordination are in danger of becoming vogue words, but what they stand for is what is urgently needed in the practice of medicine to-day. The Minister of Health sees this work of integration and co-ordination in clinical work as the responsibility of the general practitioner. This is no novel conception; general practitioners have for years consistently pressed the Ministry for just those facilities and responsibilities which the Minister of Health now says should be theirs as of right. Mr. Macleod has driven it home in direct terms at a time when this was needed. General practitioners will be eager to respond to his challenge, and in doing this they will feel encouraged to look at their work, and the way they do it, in a fresh perspective—a perspective in which the N.H.S. becomes one instead of three separate services developing independently of each other.

COMPLICATIONS OF DIABETES

The complications of diabetes may affect any system of the body, and relatively few diabetics escape them completely. Elsewhere in this issue, for example, Drs. C. Hirson, E. L. Feinmann, and H. J. Wade report finding neurological abnormalities in 57 of 100 unselected diabetic out-patients; and Semple[1] found evidence of arterial disease in 42 of a similar series of 100 patients. The designation of the various non-metabolic lesions of diabetes as complications has been criticized on the grounds that there is often no relation between the duration and severity of the diabetes and their onset, and in fact that they often appear before the symptoms of the so-called primary disease. Beaser[2] found that only 65 of 190 diabetics (34%) had classical diabetic symptoms at the time of diagnosis, and in 36 (19%) diabetic complications were the presenting complaint. There are two possible explanations for this apparent paradox. The clinical onset of diabetes may be preceded by a long silent phase during which pathological changes develop in different parts of the body. Colwell[3] went so far as to deduce from a study of insulin requirements at different ages and at different stages of the disease that diabetes begins at birth and has run half its course before it is recognized clinically. The alternative theory, supported by Dr. Wade and his colleagues, is that the metabolic upset is but one manifestation of a more general process and that the manifold effects of diabetes arise from a common unknown aetiology. The answer should be found in studies of the relative incidence of so-called complications in patients with well and poorly controlled diabetes, but here the evidence is conflicting. Wilson, Root, and Marble[4] found that, whereas 62 of 247 young patients with long-standing diabetes (25%) had diabetic nephropathy, all the 37 patients who had achieved good control of their diabetes had escaped it. On the other hand, Croom and Scott[5] found no correlation between retinal and vascular changes and the severity or control of the diabetic state.

Wade and his colleagues classify the diabetic neuropathies into three clinical groups: first, hyperglycaemic neuropathies, characterized usually by pain and paraesthesiae without objective signs and quickly relieved by control of the hyperglycaemia; secondly, active neuropathies, more severe and complex neurological syndromes with a striking tendency to relapse and remission unrelated to alteration in diabetic control; and, lastly, asymptomatic neuropathies, found in 54% of their out-patients and characterized mainly by areflexia in the legs, absence of vibration sense and deep pressure sensation, and, sometimes, abnormal pupillary reactions. On page 1405 Drs. Hugh Garland and D. Taverner report under the title "Diabetic Myelopathy" five cases of a syndrome originally described in 1890 by Bruns. The patients were between the ages of 56 and 73, and all had relatively mild diabetes of short duration, the longest history being three years. All complained of severe pain in the legs, always symmetrical and tending to be greatest in the hip and thigh. The leg muscles were wasted and there was impairment or loss of the tendon reflexes in all five patients; three had unequivocal extensor plantar responses; none had any objective sensory disturbance; four had raised protein in the cerebrospinal fluid. The authors suggest that the cord changes responsible for this syndrome may well be secondary to atheromatous degeneration of the spinal arteries. The complete recovery of four of the patients when their diabetes was controlled is perhaps against this theory: and Wade and his colleagues concluded that there was no evidence to incriminate either arteriosclerosis or vitamin B_1 deficiency as causal factors in their cases. Whatever the cause of these neuropathies, the very rare association of diabetes with Friedreich's ataxia, reviewed in this issue by Drs. D. W. Ashby and P. S. Tweedy, appears to be genetically determined.

Some practical points emerge from consideration of the complications of diabetes. The importance of routine urine testing, whatever a patient's presenting complaint, should hardly need stressing; but even in

1 *Lancet*, 1953, **1**, 1064.
2 *New Engl. J. Med.*, 1948, **239**, 765.
3 *Arch. intern. Med.*, 1942, **70**, 523.
4 *New Engl. J. Med.*, 1951, **245**, 513.
5 *Lancet*, 1949, **1**, 555.
6 Rath, C. E., and Finch, C. A., *J. clin. Invest.*, 1949, **28**, 79.
7 Houston, J. C., and Thompson, R. H. S., *Quart. J. Med.*, 1952, **21**, 215.
8 *Lancet*, 1953, **1**, 766.

the absence of glycosuria a blood sugar curve may occasionally be helpful in diagnosis. Secondly, full clinical examination of all diabetics at regular intervals is clearly essential. Not only will this often lead to the finding of lesions in the nervous system, the vascular system, the eyes, and the kidneys, but now and then it will bring to light an associated disease such as haemochromatosis. This condition is probably not so rare as was formerly thought, its recognition has been simplified by the discovery of characteristic serum iron changes,[6 7] and its early diagnosis assumes more importance in view of the possibility of treatment by phlebotomy, to which Houston[8] recently drew attention.

ANTIBIOTICS IN NATURE

The publicity given to the intensive search for new antibiotic-producing organisms during the past decade has tended to obscure the biological role of antibiotics. Microbiologists have been interested in the general phenomena of the action of micro-organisms on one another since the first serious attempts to cultivate them were made,[1] and both beneficial and harmful relations were recognized and studied before any specific stimulatory or inhibitory metabolic products were isolated. The battles often so strikingly displayed on laboratory culture media probably also took place under natural conditions in the soil, and plant pathologists were quick to appreciate that their study might lead to new methods of controlling plant diseases, especially those caused by soil-borne root-parasites. For example, Weindling[2] found that the soil fungus *Trichoderma lignorum* produces a lethal substance which enables it to parasitize a number of pathogenic fungi. Attack on *Citrus* seedlings by *Rhizoctonia solani* in sterile soil was largely prevented by adding spores of trichoderma to that soil. Other examples of this kind have been recorded in the vast literature that has accumulated.[1 3] As a result of all this work it is now known that several different kinds of antagonistic association take place in culture or in soil.

Direct parasitism of one organism by another is a form of antagonism, and many examples of it have been found among the fungi.[2] For example, species of *Piptocephalis*, moulds belonging to the Mucorales, are obligate parasites on other moulds of the same order. However, the majority of soil fungi are saprophytes and exert antagonistic effects in other ways.[4] Many fungi are able to suppress the development of other organisms by bringing about growth conditions generally unsatisfactory to them. They produce simple chemical compounds —e.g., citric acid, ammonia, carbon dioxide—which are in a sense antibiotics but act non-specifically and mainly by causing large changes in soil acidity. Other fungi —e.g., *Penicillium* spp.—and particularly filamentous actinomycetes of the genus *Streptomyces*, produce specific inhibitors, toxins, and lytic enzymes (true antibiotics). Finally, competition between micro-organisms for some limiting nutrient is also a factor which may retard their growth and may affect some organisms more than others in the mixed population.

The effects of antibiotics are frequently so striking in culture that they might well be thought to be very important in nature in controlling the microbial populations in soils. However, soil is complex and heterogeneous, both chemically and in physical structure, and in it exist vast numbers of organisms of many types in very close association with each other. All types of antagonistic and beneficial association are taking place at once, and it is impossible with present techniques to disentangle the different effects and assess their relative importance. Antibiotics undoubtedly will be produced in certain soil conditions, but it is less certain that the organisms producing them will benefit by it. Many antibiotics are inherently unstable and unlikely to persist; they may be adsorbed on to soil particles, and they are often broken down enzymatically by other micro-organisms not susceptible to their inhibitory action. For instance, Daines[5] found that a substance produced by *Trichoderma lignorum* was toxic to *Streptomyces scabies* (the organism causing scab of potatoes) in artificial liquid medium but was rapidly destroyed when added to soil.

The artificial addition of antibiotics in quantity to the soil might prove of value in farming or horticulture, but in view of the complexity of soil the prospects are not very bright. Very little work has so far been done in this direction, and it is not known what changes in soil fertility or partial sterilization might be induced. The converse process, artificial addition of living bacteria, has, however, been studied in the hope that organisms capable of producing antibiotics against the added bacteria would be stimulated to develop. Enrichment of soil in this way does usually lead to the enhanced development of various groups of organisms in it, and in some cases new antibiotics have thus been found. Dubos[6] added various pathogenic cocci to soil at intervals over a period of two years and succeeded in isolating *Bacillus brevis*, which produced antibiotics (gramicidin and tyrocidin) active against them.

However, in general there is very little proof that organisms so stimulated have necessarily produced or are able to produce antibiotics against the introduced organism. Indeed, it is difficult to see why the ability of one organism to produce an antibiotic against another should encourage it to develop in the presence of its victim, unless it is also able to utilize the cell substance of the inhibited organism. This has been shown to occur at least in culture with some of the myxobacteria, which not only produce a bactericidal secretion but a lytic substance which enables them to draw their nutrients from lysed bacteria. Have antibiotics a significance in evolution? So far it has not been possible to prove that those formed naturally in soil can influence the balance of microbial populations there, and therefore ability to produce an antibiotic is unlikely to favour the survival or development of the organism which makes it. Antibiotics may be only excretion products which accidentally at the most confer advan-

[1] Waksman, S. A., *Microbial Antagonisms and Antibiotic Substances*, 1945, New York.
[2] *Phytopathology*, **24**, 1153; *Botanical Review*, 1938, **4**, 475.
[3] Garrard, E. H., and Lochhead, A. G., *Scientific Agriculture*, 1938, **18**, 719.
[4] D'Aeth, H. R. X., *Biol. Rev.*, 1939, **14**, 105.
[5] *Amer. Potato J.*, 1937, **14**, 85.
[6] *Proc. Soc. exp. Biol. (N.Y.)*, 1939, **40**, 311.

tage by cutting down the competition for available foodstuffs. As yet it is not possible to pronounce definitely, and the biological role of antibiotics remains somewhat of a mystery.

PROGNOSIS IN DIABETIC PREGNANCY

The successful solution of a problem in medicine often brings in its train other, if less serious, problems. So ith diabetes mellitus: the adequate treatment of it by insulin has provided an increasing number of pregnant diabetics to perplex physician, obstetrician, and paediatrician. In a paper at p. 1413 of this issue of the *Journal* Dr. Wilfrid Oakley has concerned himself with the outlook for the pregnant diabetic and her baby. He confirms that the insulin requirement usually rises after the fourth month of pregnancy at a time when the renal threshold for sugar usually begins to fall. This may lead to heavy glycosuria and severe ketosis in a previously well-controlled diabetic, but with proper supervision there should be no maternal deaths from diabetic coma. Oakley found it difficult to assess the remote effects of pregnancy on the march of the disease, because increased insulin requirement, retinitis, and hypertension and albuminuria can all occur independently of an intervening pregnancy, but he does not consider that pregnancy increases the chances of such complications developing. In particular he concludes that toxaemia of pregnancy does not involve a greater risk in the diabetic than in the non-diabetic of precipitating permanent hypertension.

But if the outlook for the pregnant diabetic in terms of mortality and morbidity continues to improve, the prognosis for the baby remains clouded by a foetal loss of over 25%, a high rate which Oakley finds largely unexplained. He is unable to support views that the foetal loss is related to the duration or severity of the diabetes or to the age of its onset. In particular his figures deny that toxaemia is the cause of the high foetal death rate, and he therefore concludes that any form of therapy directed against toxaemia cannot appreciably increase the foetal salvage rate. This conclusion is diametrically opposed to the views of Dr. Priscilla White in Boston, as expressed most recently in a full account of 525 viable pregnancies in diabetic women treated between 1936 and 1951.[1] She considers that the four factors affecting the foetal mortality are the disturbed metabolism of diabetes, sex hormonal imbalance, the degree of maternal vascular disease, and congenital malformations. She emphasizes that the second of these is at least as important as the first, for it favours toxaemia, premature labour, and intrauterine death, and that it is just as amenable to treatment. The hormonal imbalance is said to be characterized by a high level of serum chorionic gonadotrophin, a low level of serum oestrogen with abnormal ratios of its degradation products, and a low level of urinary pregnanediol excretion—findings which have not been fully confirmed by others.[2] This imbalance is said to be correctible by the administration of increasing doses of stilboestrol and progesterone, which for the best results must be given parenterally; the response to them can be assessed by laboratory tests. The theoretical basis for this hormone therapy is not generally accepted, and it is interesting to note there has been some change in emphasis from the claimed stimulative effect of such treatment on the placenta to its substitutional value. Yet the results in White's treated group, in which hormone therapy was a very important but not the only feature of management, are remarkable, 345 out of 380 babies being born alive. Consequently the results of the current controlled investigation by the Medical Research Council in this country into the value of such hormone treatment are eagerly awaited.

If Oakley and White differ on the question of treatment with oestrogen and progesterone, they apparently agree on several other points of management. Thus, although others may disagree,[3,4] they both regard caesarean section at about the 37th week of pregnancy as the method of choice for delivery. One result of this interference is to shift the emphasis from stillbirths to neonatal deaths. Discounting the importance of hypoglycaemia, and disregarding those deaths due to congenital malformations, both agree that neonatal death most often occurs within 72 hours of birth and is usually due to respiratory failure, which White attributes to hyaline membrane disease. This is a field of neonatal paediatrics which requires further illumination, and it is encouraging to note that research is being pressed forward both in London and in Boston.

CHRONIC OTITIS EXTERNA

The term chronic otitis externa covers a multitude of different clinical appearances, though with few exceptions the essential lesion is an eczematous inflammation of the skin lining the meatus and concha. At one time chronic middle-ear discharges were commonly seen, and it is perhaps surprising that the skin of the external meatus was not more often the seat of pyoderma. Indeed, otitis externa is limited in most cases to the outer third or cartilaginous part of the meatus, the inner part and the drum remaining healthy.

The affection is most often seen in middle adult life and is probably more common in men. Scalp dandruff and other signs of the seborrhoeic state are often present, and when the eruption extends from the meatus to the concha and the neighbouring skin of the neck and face it usually takes on the characteristic appearance of that disease. But this is saying little more than that such a patient appears to be particularly susceptible to eczematous eruptions with local, low-grade, superficial infection of the skin; he is at the same time particularly liable to develop epidermal sensitivity and to give adverse reactions to antiseptics and antibiotics applied locally. Of the underlying nature of the seborrhoeic diathesis, of its relation to endocrine function, diet, and infections of the upper respiratory tract, there is no precise knowledge.

Otitis externa often starts insidiously with a slight scaling and irritation of the outer part of the meatus, accompanied by scalp dandruff and possibly low-grade seborrhoeic dermatitis of the head or trunk. The skin

[1] *Transactions of the Fifth American Congress of Obstetrics and Gynecology*. p. 402. St. Louis: Mosby. 1952.
[2] Keltz, B. F., *et al.*, *Sth. med. J. (Bgham, Ala.)*, 1950, **43**, 803.
[3] Bastiaanse, M. A. van B., and Sindram, I. S., *J. Obstet. Gynaec. Brit. Emp.*, 1951, **58**, 996.
[4] Barns, H. H. F., and Morgans, M. E., *British Medical Journal*, 1952, **1**, 1058.

of the meatus is tightly bound down to the cartilage, leaving little room for oedema swelling. It is well known that severe pain may result from comparatively slight oedema of the meatus, and it seems likely that irritation is also accentuated. Scratching is violent and paroxysmal, and paves the way for secondary infection. Emotional tension will usually increase itching and scratching, so that the patient's mental attitude may assume great importance and account for the intractability of the otitis.

For some years past it has been said that fungus infections are common in this situation, though current experience in the United Kingdom does not seem to support this view. More often the common streptococcus and staphylococcus are responsible, and since antibiotics began to be used *Pseudomonas aeruginosa*, which is resistant to them, has often been found. Scratching, the mild trauma of dressings, and ear-syringing may all predispose to the development of secondary infection, and exacerbations often seem to result from exposure to water in swimming. Periodically infection of the epidermis spreads to the dermis and subjacent tissues with the production of cellulitis, which may be exceedingly painful; localization of this to actual furunculosis is unusual. The occurrence of secondary infection, seeming to prolong and exacerbate the original disorder, naturally suggests treatment with antiseptics and antibiotics. But if this treatment is continued for more than a few days epidermal sensitization to the application is apt to develop, resulting in a rapid spread of weeping dermatitis to the pinna and surrounding skin. When this stage is reached the aetiological factors are confused and may be most difficult to unravel. It is then far easier to do harm with treatment than good.

Treatment is almost entirely a matter of local applications, but great caution should be exercised in the use of local antiseptics. The common hospital practice now is to identify infecting organisms in culture, to determine their antibiotic sensitivities, and to give treatment accordingly. Although this is, no doubt, the theoretically correct procedure, it is doubtful whether in practice it yields particularly good results. Organisms seem to change their sensitivity, and superinfection with resistant organisms so readily occurs, that better results are often obtained with antiseptics having a wider bactericidal effect. Proprietary preparations containing chlorhydroxyquinoline or iodochlorhydroxyquinum ("quinolor" cream and "vioform" cream) seem at present to offer a good compromise between antiseptic activity and the possibility of irritation or sensitization. Even so, it is probably best to limit their use to a few days while the worst of the infection is overcome, and to cease the application before the skin has had time to become sensitized. Four or five days' antiseptic treatment is nearly always safe and is nearly always sufficient. After this the treatment is that of eczematous dermatitis and varies according to the degree of activity of the inflammatory process. At all stages emulsified bases such as unguentum aquosum *B.P.* are likely to be preferable to purely greasy applications, though in the more chronic stage Lassar's paste can hardly be bettered. As an antipruritic 2% or 3% liquor picis carbonis may be added to the application. The antihistamines have proved, as was expected, to be inclined to cause epidermal sensitization and contact dermatitis when applied locally; their use in otitis externa involves considerable risk of this complication and is seldom advisable. *X*-ray treatment can be extremely successful. It is probably best withheld until the condition has reached a quiescent stage, whether with treatment or spontaneously, when repeated small doses of superficial *x* rays will often prevent recurrence.

POISONOUS FISH

Such scientifically highly civilized parts of the world as the British seaside are virtually free of fish lurking to sting or lacerate the unlucky bather. Nor do the sea fisheries of Western Europe trawl up fish poisonous to eat, and anyone who has been served with a Mediterranean fritto misto of starfish, sea cucumber, squid, and other members of the molluscan, arthropod, or echinoderm phyla will testify to the fact that most sea creatures are amazingly innocuous to the digestion. But it is otherwise in the Tropics. The director of fisheries in Malaya recently lectured[1] to the Malayan Branch of the B.M.A. on the various kinds of catfish, sting rays, and scorpion fish provided with sharp spines and puncture poisons of unknown composition, and on the puffer fish, which blows itself up like a football when disturbed and is dangerous to eat. Sea snakes also are common around Malayan shores, the commonest species being four or five feet long and its venom eight times as poisonous as that of the cobra, of which it is a relation. It is good to know that "sea snakes are gentle and inoffensive creatures, and do not bite unless they are provoked."

The treatment of injuries caused by fish appears to be best carried out by sucking out the poison and spitting it away, opening up of the wound as quickly as possible, and washing with permanganate. Cortisone may be a useful adjuvant in severe cases, for it has been found helpful in cases of snake-bite poisoning.[2] The Malay peoples have various "cures" for catfish poisoning, some of which are herbal, and it would be interesting to know whether they have a useful pharmacological effect or are purely magical. As for the puffer, whose body contains alkaloids which produce respiratory and cardiac failure, it is apparently a Japanese delicacy. If all its viscera are removed immediately it is caught it is said that the poisons have no time to diffuse into the adjacent flesh, which is then quite wholesome. But accidents have been recorded.

At the annual general meeting of the Royal Statistical Society on June 24 the Guy Medal in Gold was awarded to Professor A. Bradford Hill, who, in the words of the report of the council of the Society, "has occupied for many years a pre-eminent position in the field of medical statistics, in which he commands the highest regard not only in this country but also overseas. It was a tribute to his international reputation that he was recently elected an honorary fellow of the American Public Health Association 'in recognition of his outstanding services in the field of public health.'"

[1] Le Mare, D. W., *Med. J. Malaya*, 1952, **7**, 1.
[2] Hoback, W. W., and Green, T. W., *J. Amer. med. Ass.*, 1953, **152**, 236.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

BREAST-FEEDING DIFFICULTIES

BY

F. CHARLOTTE NAISH, M.D.

Feeding difficulties fall naturally into two divisions: overfeeding and underfeeding, but the former is far less common and less important than the latter. When the supply of milk is abundant and it flows freely an active, greedy baby may take too much. Perhaps six out of ten of these babies promptly vomit the excess and make normal gains in weight; these present a laundering difficulty but not a feeding difficulty. Perhaps two more retain the excess and make exceptional gains in weight: as the food is well balanced, the growth is well balanced, and so, again, there is no feeding problem. The remaining two babies may suffer from frequent loose stools, through overloading their stomachs. Since frequent loose stools are also (and much more commonly) a sign of underfeeding, the first essential is to verify by test-weighing that the baby is really taking an exceptional quantity. If this is found to be so, then no immediate treatment is necessary, for the condition is not serious and usually rights itself. In no case should treatment aim at reducing the milk supply, for such treatment nearly always overreaches itself and creates an underfeeding problem. If it is considered essential to reduce the bowel action, this should be done by giving an emulsion containing 2 minims (0.12 ml.) of castor oil and 20 gr. (1.3 g.) of mucilage of acacia to the drachm (3.5 ml.) of water. One drachm before feeds is a suitable initial dose, and the dosage can be freely varied according to the result obtained.

In all other cases of difficulty the baby gets too little milk.

Recognition of Underfeeding

The number of babies classed as underfed will depend largely on the doctor's standard of satisfactory weight gain. There is wide variation in this. From the fourteenth day to the end of the third month the weekly gain is independent of the birth weight and should not be less than 6 oz. (170 g.). Eight ounces (230 g.) is a reasonable target for boys and 7½ oz. (210 g.) for girls. This does not mean that these gains can be looked for every week: such progress often occurs, but probably cannot be ensured in any way. But it does mean that every baby gaining less than 6 oz. (170 g.) is to be classed as momentarily underfed, and corrective measures applied so that it shall gain from 18 to 24 oz. (500 to 700 g.) in any and every spell of three weeks. It is not enough merely to get back to gains of 6 oz., but the arrears should also be made up.

Though it is true that loose greenish stools are generally a sign of underfeeding, the bowel signs are ambiguous. It is better to base treatment on weight and use the return to normal stools as a check on the adequacy of the measures taken.

When dealing with mothers who are not satisfied with the progress of their babies, one must remember that the babies are under constant observation by people who are concerned for them; in consequence the number rightly referred to a doctor greatly exceeds the number referred unnecessarily. Moreover, if the mother worries without cause it is bad for the baby; so much so that there will ultimately be a feeding difficulty if the case is dismissed without study and explanation. Often, however, the history will be overlaid with interpretation, so that in its first form it is useless: the essential facts may need to be elicited by cross-examination.

The main causes of underfeeding are mechanical difficulties, which may be in connexion with the mother, the baby, or both; infections; and insufficient flow or secretion of milk.

Mechanical Difficulties

In the baby, difficulty may be caused by *nasal obstruction.* There may be a congenital malformation of the nasal passages which, if severe, results in great respiratory distress, as the infant's reflexes are not adapted to purely oral breathing. Such cases are not primarily feeding problems, and are unsuitable for domiciliary treatment. Partial nasal obstruction may result from an upper respiratory infection, and may be treated with nasal drops before the feed. Chlorbutol and menthol nasal drops (*N.F.*, 1952) are useful for this.

Hare-lip and cleft-palate constitute a bar to feeding at the breast, but not necessarily to feeding with human milk, provided the mother is good at manual expression of her milk. Breast pumps are in general unsatisfactory because they work by suction alone, without expression. This does not produce enough milk from the breast to maintain the supply.

Tongue-tie has been so often diagnosed in error that some teachers have reacted so far as to deny its existence. Although it is rare, I believe that it does occur and is well worth treating. Part of the process of getting milk from the breast consists in compressing the nipple against the palate by drawing the tongue along it. Occasionally the tongue is not mobile enough to carry out this movement. In some babies labelled "bad suckers" it can be observed that the tongue never comes forward beyond the lower lip or, in extreme cases, beyond the lower gums, and, as a confirmatory sign, the tongue does not point normally in the forward position, but shows a double curve and central recess. If the fraenum of such a tongue is snipped the tongue will point normally—sometimes at once but more usually after about three days. The "bad sucking" is completely cured.

In the mother, *malformed nipples* are a fairly frequent cause of difficulty. If observed early they can be cured by the wearing of "Woolwich-type" nipple shields for the remainder of the pregnancy. Even if the condition is not observed until near the confinement it is still worth ordering the shields; though, as their action is gradual, they will not be nearly so effective.

If the practitioner does not see the mother until the nipples are actually causing difficulty in feeding, then the matter is serious. A breast pump may sometimes be applied just long enough to draw out the nipple to its fullest extent, and the baby immediately substituted; but this will not be enough in severe cases. The most generally applicable method of feeding an infant on human milk when the mother's nipples are not usable is for her to express the milk by hand. Her ability to do this well usually depends on her having practised daily expression of colostrum for six weeks or so before the confinement. A breast pump should not be used to obtain milk, for the reasons given above. Faulty nipples, if not treated in time, may spell defeat, even though everything else is propitious.

Cracked nipples are even commoner than malformed nipples, and, like them, can be almost entirely avoided; if they occur, they constitute a very serious difficulty. The two main causes of cracked nipples are: (1) failure to keep the skin soft by oil-massage during pregnancy and, in the worst cases, deliberate hardening by scrubbing and spirit lotions; and (2) excessive suckling during the first three to four days after the birth, before the milk has "come in." It is most regrettable that much traditional teaching advocates both these faulty procedures.

A cracked nipple cannot heal while it is in use, so that suckling must be temporarily given up. Also, every cracked nipple is liable to infection and needs to be softened—ends which can be met by the exhibition of penicillin cream during the resting period. If there is a yield of milk to be preserved manual expression should be performed. The breast pump is even more definitely contraindicated than in the treatment of malformed nipples, for the suction, in elongating the nipple, opens the crack, and is just as painful as suckling. Nipple shields of the type through which the baby sucks are to be classed as pumps in these respects. If cracked nipples due to both hardening of the skin and excessive sucking coincide with engorgement the position is more serious still, as the epithelium of the nipple becomes oedematous and liable to further damage.

Some degree of *engorgement* is usual between the third and tenth day after birth. If it is severe and not properly handled the breasts may become swollen, hard, hot, and superficially oedematous. The areola, under which lie the main collecting sinuses, will be too taut for the baby to grip and squeeze between its jaws, and in consequence feeding is impossible until the tension subsides. This will happen after two or three days; but those are days of starvation for the infant, of acute discomfort with a high liability to mastitis for the mother, and of internal damage probably leading to partial involution for the breasts themselves. Treatment is therefore advisable, and the most effective method of shortening the engorgement is the exhibition of stilboestrol: three doses of 5 mg. at four-hourly intervals. In the most severe cases a larger first dose, up to 20 mg., has been recommended. Stilboestrol treatment is suspected of having some permanent effect on the lactation in a fair proportion of cases, but it reduces the danger of mastitis and the period of starvation.

If the doctor is at hand at the beginning of engorgement, then the best way of forestalling the acute phase is to institute a regime of frequent but short feeds, perhaps two-hourly feeds of five minutes each side. The baby is usually hungry enough at this stage of its life to accept such a regime and feed vigorously, provided that its rest is not cut down too much; this is one reason for keeping the feeds short. Such feeds may be followed by careful expression by hand (by the mother, because she is less liable to damage the underlying tissues), but care should be taken to see that she does not get too anxious and exhausted. This regime is most sucessful when it has been explained in the course of antenatal education: it is quite impossible if, at the same time, the nipples have been allowed to become cracked.

Infections

Many babies with infections do not present only a feeding difficulty, and the doctor will quickly sort out those with a frank pyrexia, with obvious respiratory difficulty, or with acute diarrhoea. However, the class of infected babies includes many more than these. There are many mild infections which are very difficult to recognize. On the whole subject of infection in infancy, no one should omit to study Cruickshank (1945) and Moncrieff (1953). A history of loss of appetite, or of vomiting of sudden onset, or of offensive stools is suggestive of an infection; abnormal redness of the mucous membranes or of the finger-tips (as though a number of whitlows were forming) is a sign pointing in the same direction. There may not be actual loss of weight, but the gain is sure to be low. Many such infections pass unrecognized.

The treatment of an infection should be the immediate exhibition of penicillin by injection, in doses of 300,000 units (suspended) every 24 hours. Without prejudice to the question of how antibiotics should be used in adults, there must be no delay in giving them to infants, in whom an infection may not provoke any physiological reaction.

Inhibition and Failure of Lactation

It may be difficult to distinguish clinically between inhibition of the flow of milk and failure of secretion as causes of underfeeding.

If, when the baby is taken away from the breast after about two minutes, milk is seen to be squirting from the nipple it can be assumed that there is no inhibition of the flow of the milk. This simple test is either positive or indecisive, never negative. On the other hand, if a baby takes the breast eagerly, but soon refuses to suck, cries vigorously, and will not make another attempt, it can usually be assumed that the contraction of alveoli and ducts in response to the stimulus of sucking has been inhibited. Once more the absence of this behaviour means nothing. The time at which underfeeding occurs is some guide to the probable cause. Since the growing baby demands more and more milk, the later underfeeding occurs the more likely it is to be due to a lack of active tissue in the breast. The same line of reasoning indicates that a gradual drop in the baby's gains is probably due to inadequate secretion; a sudden drop to inhibition of flow.

The causes of inhibition of flow are psychological, but fortunately they are usually superficial. It is extremely common at the moment when the mother takes sole charge of the infant and at the same time resumes her household duties. Worries quite unconnected with the nursing couple may inhibit the flow at any time. So may uncongenial people in the entourage; a midwife or mother-in-law may easily prejudice the success of breast-feeding.

Either cause of underfeeding may produce the other. If the mother is worried because the baby's growth is slowing down, this may add failure of flow to failure of secretion. And if the inhibition of flow, when secretion is plentiful, leads to stretching of the breasts the secretion will be reduced. In addition, underfeeding through failure of the flow is a self-aggravating condition—that is, the fretfulness of the underfed child worries the mother and so prolongs her inability to give the milk which is present in the breast. This underlines the need for prompt and firm treatment when a baby is gaining insufficiently; it is important to deal with the situation before secondary causes come into operation.

Treatment of Underfeeding

The first line of treatment is complementary feeding. Provided a good technique is used (see below) this method will ensure immediately an adequate intake, with the highest possible proportion of human milk, it will ease the mother's anxiety, and permit a return to full breast-feeding if the flow or secretion of milk is restored. It is also largely self-regulating.

Other treatment may also be required. If the mother is nervous or the baby cross, sedation may be advisable; for the baby syrup of chloral, 15 minims (0.9 ml.), should be given half an hour before the feed. If inhibition of the flow of milk from the gland is the cause of underfeeding, some psychological exploration of the situation will be necessary. Simple measures, such as feeding in physical comfort, in solitude and quiet, and without haste at the start, are often all that is needed. If the secretion is inadequate the mother's output will be increased by shortening the interval between the feeds, for this keeps the gland in full activity for more of the day. The length of the feeds should not be increased: it may have to be cut down if the frequency of feeding is reducing the baby's sleep. In a few cases of only slight underfeeding, treated early, this method may take precedence over complementary feeding. In cases in which failure of flow is the primary cause of underfeeding there is no indication for feeding more often, and to do so might increase the tension already present in the situation.

The technique of complementary feeding deserves careful attention. Any normal artificial-feeding formula will serve for the complement, for, though the baby is unaccustomed to any but human milk, the amount of complementary feed that it will have to take is usually small. The complement should be offered immediately after the breast-feed; it must therefore be prepared beforehand and kept warm during the feed. It should be given by spoon from a cup; the quantity to be given is what the infant will readily take. If the complement is given from a bottle, only the second of the four

purposes of complementary feeding (allaying anxiety) will be fully achieved. There have been disputes on this question, and many cases have been cited in which an adequate intake was immediately secured and the mother's anxiety was allayed. But no cases have yet come to my notice in which the proportion of human milk in the diet was the highest possible or in which a return to full breast-feeding was practicable without a sacrifice of weight gain.

Conclusion

Finally, brief mention must be made of three conditions which may worry either the doctor or the mother—namely, failure to establish lactation, vomiting, and constipation.

Non-lactation is often diagnosed too soon. It is important at all times to give sips of sterile water (with or without sugar) to allay the baby's thirst, as this interferes with its rest more than hunger does. But artificial feeds should not be given until the eighth day or until the baby has lost 15% of its birth weight, whichever is the earlier; and they should not exceed 1 oz. per lb. (60 ml. per kg.) of body weight a day until the fourteenth day. If by that time the milk is still not coming in in effective quantities it may be doubted whether lactation can be established.

Vomiting is a constant cause of complaint. Few mothers (strange though it seems) expect milk to be curdled in the stomach, so that the curds in the vomit alarm them. Vomiting should be judged in relation to test feeds and weight gains. If it seems that the baby's progress is affected by the vomiting, and there is no infection, then belladonna, 5 minims (0.3 ml.) of the tincture in water, or atropine methonitrate, 2 to 5 drops, should be given before the feeds. Even when the infant's progress is not affected, this treatment may be necessary to quieten the mother. If the vomiting continues in significant quantity, a stomach wash-out should be given to determine whether there is mucous gastritis; if large quantities of mucus are found the treatment should be repeated daily until the condition remits. The only cases of vomiting needing weaning are those which follow on puerperal sepsis.

Constipation is usually a false report. What is nearly always meant is that the motions are infrequent, but the stools are normal in themselves and passed without strain. The condition demands no treatment whatever. In the rare cases in which the stool is hard and difficult to pass (and pyloric stenosis has been excluded) a mild laxative should be given, such as mist. magnes. hydrox., *B.P.*, ½ to 1 drachm (1.7 to 3.5 ml.), or syrup of senna, 15 to 30 minims (0.9 to 1.8 ml.).

The number of points at which prevention is not only better than cure but also much simpler is worth stressing. Regular supervision will always lead to greater success than can be secured by interventions to deal with difficulties.

REFERENCES

Cruickshank, R. (1945). *Arch. Dis. Childh.*, **20**, 145.
Moncrieff, A. A. (1953). *British Medical Journal*, **1**, 1.

Next Refresher Course Article.—"Pyelitis in Children," by Professor A. V. Neale.

The Treatment of Accidental Poisoning.—In the paragraph on the treatment of aspirin poisoning in this Refresher Course article (May 30, p. 1214), the use of "intravenous sodium lactate (70%)" is advised. In order to obviate any possibility of misunderstanding, it should be stated that the sodium lactate is to be given in *isotonic solution*. The 70% refers to the strength in which the lactate is usually purchased.

Refresher Course Book.—The first collection of articles of this series (fully revised) are available as a book containing 55 chapters, price 25s. Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from your bookseller.

LINGUA MEDICA

A STUDY IN MEDICAL SEMANTICS*

BY

FFRANGCON ROBERTS, M.D.

Socrates: He who first gave names gave them according to his conception of the things which they signified, and if his conception was erroneous . . . shall we not be deceived by him?—PLATO, *Cratylus.*

The meaning of anything is usually another name for the same thing.—CHARLES CHAPLIN, *Limelight.*

The language of medicine has more than utility value. It enshrines the ideas about disease which were held by primitive societies, the gradual evolution of medical knowledge in 2,500 years, and the geographical course which this knowledge has taken. It illustrates the mental processes by which men in all ages have found names for natural phenomena, incidentally giving us glimpses of their domestic, agricultural, and military background, and it explains why medical concepts, however modern, are still most accurately expressed in the language of Hippocrates.

Sources

The principal sources of medical words are five: Saxon, Graeco-Roman, Romance, Arabic, and Modern German.

Saxon

This source comprises our native Anglo-Saxon, together with Scandinavian, Teutonic, and other languages of North-west Europe. The words which it furnishes are all short, and express simple ideas—*head, hand, ache.* Their derivation is of no interest except to students of these languages.

Graeco-Roman

This is, of course, the most prolific source. The Greek component derives from early Greek, Minoan, Egyptian, and Asiatic sources, and first appears in organized form in the writings of Hippocrates (b. *circa* 460 B.C.). On the decline of Greece proper the words were taken over by the Greeks in Alexandria and later by the Romans. The Romans were in the habit of employing Greeks as their physicians, among them Galen (A.D. 131–200), but they also practised medicine themselves either as professionals or as amateurs. The head of a household, at any rate in the provinces, would dispense medicines to the members of his villa. But whether Greek or Roman, professional or amateur, they were bilingual, and used Greek and Latin words according to convenience. This explains the double nomenclature of the present day: *nephros, ren; orchis, testis; encephalon, cerebrum.* Andrews (1947) maintains that Latin words were completely suppressed except for a few such as *anus, penis*, which might be used in vulgar jokes. This is manifestly incorrect, as the writings of Celsus and others abundantly show.

Romance

Romance words are those which, though of classical derivation, arose in Italy, France, or Spain. From Italy we have *belladonna* (beautiful woman, from the effect of the drug on the eyes), *malaria* (bad air), and

* In this article the following abbreviations are used: Ar., Arabic; E., Modern English; M.E., Middle English; F., Modern French; O.F., Old French; G., Greek; L., Latin; Lit., Literally; Pop., Popular.

influenza. From France come *goitre, tic douloureux, grand mal, petit mal, chancre, trocar,* and many others. From Spain, *mosquito* and *quarantine*.

Arabian

During the long eclipse of Western culture in the Middle Ages (A.D. 476–1453) science was pursued to a high level by the Moslems, whose empire extended from Arabia, through Egypt and the north coast of Africa, to Spain. To them we owe algebra and our arithmetical notation. They translated the Greek and Latin medical texts, the use of which was proscribed by the Christian Church. At the Renaissance the Humanists, experiencing great difficulty with the Arabian translations, and finding a new pride in their long-neglected heritage, sought the original sources. Consequently few Arabian words survive. Most of these are names of chemical substances: *sugar, syrup, alcohol, alkali, elixir, naphtha, senna.* Of medical words there seem to be only four:

Nucha, neck.

Mater (dura and pia), from the Arabic word for *mother*. The Arabians were, and still are, in the habit of using flowery language, with a special preference for family relationships. *Mater* therefore means either mother of membranes or, more probably, mother or protector of the brain.

Cephalic (vein), from Ar. *alkifal,* outer.

Basilic (vein), from Ar. *basilik,* inner.

The *Oxford English Dictionary,* however, derives *cephalic* from the belief that this vein influenced the head, and *basilic* from the fact that this was the chief, therefore royal, vein used for bleeding (G. *basileus,* king). With all due respect I think the Arabian origin the more probable.

Modern German

For reasons given below these are very few—*magenstrasse, magenblase,* the hybrid *kernicterus,* and some psychiatric terms.

Corruption

In their migration across Europe many words have become corrupted. In some—for example, *shingles,* from *cingulum,* belt—the phonetic resemblance is obvious. In others, the process is more gradual. L. *botellus,* pudding or sausage, late pop. L. small intestine, O.F. *boel,* M.E. *buel* or *bouel,* E. *bowel.* G. *plege,* a blow, L. *plaga,* O.F. *plage,* M.E. *plage,* E. *plague. Hydropsie, dropsy.* Cf. pop. *polio, flu.*

The Construction of Modern Words

In constructing modern words classical words are invariably used, never the Saxon. For this there are several reasons. First, Saxon words go no further than primitive folk-medicine. In the classics, on the other hand, we have an elaborate verbal system invented for much more advanced concepts. Moreover, until the eighteenth century Latin was the universal language of scholarship. Secondly, by using classical words medicine allies itself with other sciences. *Proto-,* first, is used in physics and medicine; *cortex* and *medulla* are used in botany and medicine.

Thirdly, in English, minor parts of speech—pronouns, prepositions, and auxiliary verbs—play an essential part. By their use main words can be kept small, a fact which contributes to the richness of our language in poetry and literature.

". . . he fell from off the seat backward by the side of the gate, and his neck brake, and he died; for he was an old man and heavy." (I Samuel, iv. 18.)

By reason of its simplicity and directness this passage might serve as a model for a medical witness at an inquest.

In describing more complicated matters, however, it is essential to eliminate minor parts of speech and to use portmanteau words. Take *agranulocytosis—a,* neg. or alpha privative; *granulum,* granule; *kutos,* cell or vessel; *sis,* a state of; a state of deficiency of the kind of cells which have granules. One word of 15 letters does for 12 words having a total of 51 letters.

Fourthly, we can express recognized diseases. *Acromegaly,* lit. large ends. To say "a man with large hands and feet" might mean anything, since many normal men are so built.

It is fortunate for us that this country stood in the stream of classical culture. The Germans, who, living too far north, were outside this stream, had to build up their medical language on their native Teutonic foundations. Hence the clumsiness of their vocabulary, which is full of such words as *zwölffingerdarmgeschwür,* twelvefingerintestineulcer for duodenal ulcer, and *wormfortsatzentzündung,* wormlikeprojectionburning, for appendicitis. International communication now compels the Germans to abandon such words for the classical.

When there is the choice of a Greek or a Latin word the rule is to use the Latin only in adjectival forms and with prefixes (apart from hyphenated words such as *cerebrospinal*), and to use the Greek when two nouns or a noun and a verb are joined. *Renal, suprarenal,* but *nephropexy*; *testicular,* but *orchidectomy.* (I exclude names of pharmaceutical preparations. With the erudition of commerce I cannot keep pace.) This practice is in the best classical tradition, since the Romans did not adopt the Greek habit of joining major parts of speech together.

Hybrid Forms

Medicine is riddled with hybrid Greek-Roman words. For instance, the G. *-itis* is suffixed to words of both languages. Despite the pundits there is no objection to hybrids (though this *Journal* might get rid of its *addressograph*). Ordinary speech would, in fact, be very difficult without them. In *On the Art of Writing,* by the late Sir Arthur Quiller-Couch, Professor of English Literature, Cambridge University, there occurs this unfortunate passage:

"I was waiting, the other day, in a doctor's anteroom, and picked up one of those books—it was a work on pathology—so thoughtfully left lying in such places; to persuade us, no doubt, to bear the ills we have rather than fly to others capable of being illustrated. I found myself engaged in following the antics of certain bacilli generically described as 'Antibodies.' I do not accuse the author (who seemed to be a learned man) of having invented this abominable term: apparently it passed current among physiologists, and he had accepted it for honest coin. I found it, later on, in Webster's invaluable dictionary: Etymology, 'body' (yours or mine, 'anti,' up against it: compound, 'antibody,' a noxious microbe.

"Now I do not doubt the creature thus named to be a poisonous little wretch. Those who know him may even agree that no word is too bad for him. But I am not thinking of *him.* I am thinking of *us*: and I say that for our own self-respect, whilst we retain any sense of intellectual pedigree, 'antibody' is no word to throw even at a bacillus. The man who eats peas with his knife can at least claim a historical throwback to the days when forks had but two prongs and the spoons had been removed with the soup. But 'antibody' has no such derivation. It is, in fact, a barbarism, and a mongrel at that. The man who uses it debases the currency of learning."

This is severe enough. But read the first sentence again. The censorious professor himself uses the word "anteroom"—a mongrel if ever there was one, half Latin, half Teutonic.

The Persistence of Obsolete Ideas

As everyone knows, the humoral theory, which dominated medicine from Greek times to the middle of the nineteenth century, is indelibly imprinted in our speech—in *sanguine, phlegmatic, choleric, melancholic,* and in *humour* itself. From the Greek age we also have *hysteria, hypochondria, phrenic* (frenzy), *spleen* (or ill-temper); the boiling out of the humours in *eczema* (G. *zeein,* boil), and the

secretion of *pituita* (mucus) from the brain through the base of the skull into the nose. The arteries, being empty at death, were believed to carry air, hence their name (G. *aer*, air, *tereo*, carry).

Derivation by Association or Transfer

Innumerable names are derived from resemblances to animals, plants, parts of buildings, musical instruments, articles of adornment, tools, and weapons. Of greater interest are words derived by association or transfer. Several types can be recognized :

1. *Transfer from the Thing or Animal Used.—Histos*, loom. In *histology* the meaning is transferred to the material made from the loom. *Vaccination*, from *vacca*, cow. *Graft*, from G. *graphein*, write, through O.F. *graffe*, F. *greffe*, and M.E. *grift*. The Gauls were taught horticultural grafting by the Romans, who used slips shaped like pencils. In *inoculate* we have a similar idea, the bud to be grafted being the "eye" (oculus)—cf. the eye of a potato.

2. *Transfer to an Attribute.—Anopheles*, harmful (insect). *Jejunum*, empty. *Trachea*, rough; originally *arteria trachea*, rough air-vessel—cf. pop. *whites* for leucorrhoea.

3. *Association Through a Common Characteristic.—Anthrax*, coal, and *carbunculus*, little coal, the common idea being burning. John of Trevisa (1535), translating the great thirteenth-century encyclopaedia, *De Proprietatibus Rerum*, by Bartholomeus Anglicus, a work probably used by Shakespeare, has : "Antrax is a postume whyche cometh of ful wood matere and venomous. It is callyd also 'carbunculus,' for it brennyth like a coal." *Alopecia*, from *alopex*, fox, the common idea being manginess. Trevisa, from the same source, has : "By that euyll callyd Allopicina nourysshynge of heer is corrupte and fayllyth, and the foreparty of the heed is bare, such men fare as foxes."

4. *Indirect Association.—Quinsy*, from G. *kuon*, dog, *anchein*, throttle, through O.F. *squinancie* and F. *esquinancie*. The idea was no doubt derived from the self-strangulation of a dog straining at the leash. At first it was applied to any obstruction of the throat. *Carotid*, from G. *karos*, sleep, from the Greek practice of producing unconsciousness by compressing these arteries—cf. F. *garrotter*. *Pupil* (of the eye) from *pupilla*, little girl or doll; so-called from the small image of oneself seen in another's eye. *Oestrus*, gadfly, a modern example. In some animals sexual excitement resembles excitement caused by a sting. *Idio-*, in *idiopathic*, *idiosyncrasy*, of course means peculiar to itself. In Greek times *idiotes* meant a private person, private in the sense that he kept himself to himself and took no part in civic affairs. Hence by easy gradations through *non-expert*, *layman*, *ignoramus*, *foolish*, to *idiot*.

Change in Meaning

Change in meaning takes various forms :

1. *Simple Change.—Asphyxia*, lit. no pulse. It retained this meaning until the eighteenth century. *Atheroma*, from G. *athere*, porridge, originally meant sebaceous cyst, from the consistency of the contents. The somewhat similar appearance of the aorta led in the middle of the nineteenth century to its present meaning.

2. *From the General to the Special.*—It has always been customary, when the true nature of a disease is unknown, to name it from its main characteristic. *Pyrexia of unknown origin* is a modern example. *Typhus*, from G. *typhos*, mist, figuratively expresses the stuporous mental state in fevers. *Eclampsia—ek*, from *lampas*, light—was first applied to any illness arising suddenly like a flash of light. *Herpes*, creeping, was applied to all spreading skin infections.

3. *From the Special to the General.—Nausea*—G. *naus*, ship—at first meant sea-sickness, but had acquired its modern meaning by the time of Hippocrates. *Thele*, nipple, has acquired a wide application in *epithelium*, *endothelium*.

4. *Complete Reversal.—Nyctalopia* was used by the ancients for day-blindness as well as night-blindness. *Phlegmatic*, cold, indifferent, comes from G. *phlegma*, burning, inflammation. The contradiction is more apparent than real. Catarrh, which was regarded as the typical form of inflammation, results in the secretion of *pituita*, mucus, which Hippocrates, in *The Nature of Man*, describes as the coldest of the humours. It is a remarkable fact that, although we use several Greek words meaning heat, we do not use *psuchros*, or any other Greek word meaning cold. Those interested in the medical aspects of Polar and Himalayan exploration have not yet learnt to call themselves psychrologists. *Symposium*, in Greek times, meant a drinking-party (for men only). High thinking was, however, far from being neglected. In fact, the purest gems of philosophy, including Plato's *Symposium*, arose in those enjoyable gatherings. The Greeks got more inspiration from their wine-cups than we get from our tea-cups.

Words of Obscure Origin

The search for origins is sometimes rendered difficult because the ancients, like ourselves, used a word in widely different meanings. In M.E., *reins* meant feelings as well as kidneys. In the former sense it appears several times in the Bible. "God trieth the hearts and reins" (Psalms vii. 9), "My reins shall rejoice" (Prov. xxiii. 16).

Amnion meant lamb and also bowl for receiving the blood of sacrificial animals. Its first application to a foetal membrane appears in the writings of that flamboyant philosopher Empedocles (504–443 B.C.), but there is no reason to suppose that he derived this use from either of its other meanings, capable though he was of supersonic flights of imagination.

Astragalos had no less than eight meanings. Both in the *Iliad* and the *Odyssey* it is used for the first or second cervical vertebra. Hippocrates gives it its modern meaning. It was also used for knuckle-bones and for any other bones used as dice in gambling.

Thymus—G. *thumos*, thyme—originally meant any warty excrescence, from the supposed resemblance to a bunch of thyme. Galen was the first to apply it to the gland. English butchers sometimes call it sweetbread of the neck to distinguish it from the pancreas, but although thyme suggests sweetness the idea that this is the connexion is too far-fetched.

Cataract, in addition to its present meaning, also meant something which impedes a cataract—namely, a sluice-gate. Ambroise Paré (1550) has *cataracte ou coulisse* (portcullis).

Misnomers

Medicine teems with verbal inaccuracies. We must remember, however, that much of medical jargon is incorporated in popular speech, and therefore partakes of the general sloppiness. Take, for instance, the word *catch*. Who does the catching and who gets caught? We say, "It catches me in the neck" and, "I caught pneumonia" (cf. F. *la grippe*, influenza). The truth is of course, that only the bacteriologists can catch the pneumococcus; the rest of us can no more catch one than we can catch a train. Then there is our incorrigible habit of blaming the environment for raining *attacks* and *strokes* upon our unoffending persons. We have an attack of indigestion when it is almost certainly our own fault. So we have *impetigo*, from L. *impetere*, attack; *epilepsy*, from G. *lepsis*, attack; *plague* and *hemiplegia* from G. *plege*, blow.

Prefixes are very often used as arbitrary means of making distinctions, regardless of their true meaning; *ortho-*, *meta-*, and *para-* in organic chemistry; *epilepsy*, attack upon, and *catalepsy*, attack down; *analysis*, loosening up, and *catalysis*, loosening down. (We say *break up* when we might as well say *break down*). Verbs, too, are used with no strict regard to their meaning; *syndrome*, running together, and *symptom*, falling together.

But, this said, there remain some words which should be suppressed. The worst offender is *haemophilia*, love of blood. Almost as bad is *parenchyma*, beside-in-juice.

Ecchymosis should be *echaemosis*, since it is blood that is poured out. *Lithotomy* should be *lithectomy*, since the stone is cut *out*. Unwarranted liberties are taken in the use of *-sis* (*-osis, -asis*). The meaning of this ending should be restricted to *a state of*, to distinguish it from *-itis*, inflammation. It can indicate an attribute, as in *cyanosis* (G. *kuanos*, blue), the presence of an abnormal constituent as in *anthracosis*, a non-inflammatory disease as in *sarcoidosis*, or a condition associated with disease as in *acidosis*. *Diverticulosis* should mean merely that diverticula are present; *diverticulitis*, that they are inflamed. In *leucocytosis* the prefix *hyper-* is understood by ellipsis. *Nephrosis*, a state of kidneys, is nonsense. *Neurosis* is no better, but can perhaps be sanctioned by the popular expression "state of nerves." *Aponeurosis*, a ridiculous word, perpetuates the inability of the Greeks to distinguish between nerves and tendons.

The Plural

In forming the plural we should be guided by general sanction rather than by strict adherence to etymology or consistency (cf. *gladioli, antirrhinums*). Since we are writing English, we may regard the classical words which we use as naturalized into English. Moreover, we cannot expect people who know little of the classics to appreciate the difference between feminine Latin nouns ending in *a* and Greek neuter nouns ending in *a*. *Stigmata* is usual, but *enemata* is pedantic. *Empyemas* is, I think, preferable to *empyemata*. In Latin nouns of the fourth declension—for example, *sinus*—which are the same in the singular and plural, the English plural avoids confusion. Incidentally, *sino-auricular* should be *sinu-auricular*.

American Usage

American usage differs from ours in the following ways: (1) Reversal of *r* and *e*; *fiber* for *fibre*. Our usage is better. (2) Suppression of *u* after *o* in such words as *color* for for *colour, humor* for *humour*. This is more correct, but our forms are too firmly established to be changed. (3) Suppression of the final *al* after *ic*; *physiologic* for *physiological*. This again is more correct, since *al* is redundant, but the position is complicated by the conversion of many adjectives ending in *ic* into nouns: *logic, economics*. Note that *economic* and *economical* have different meanings. (4) The use of *e* instead of the ligatures *æ* and *œ* (wrongly called diphthongs). The ligature is a clumsy device and causes great difficulty to typists. Moreover, *œ* fails to represent the original sound *oi*. The G. *oisophagos* was represented better by the Early English *ysophagus*. *Fetus* is better Latin than *fœtus*. I think the ligatures should be abolished. We get on quite well without them in *economy* (*oikos*, house, *nomos*, law) and similar words. In holding this opinion I find myself in the good company of Fowler.

Conclusion

"The Man of Science," said Sir James Barrie, "appears to be the only person who has something to say just now—and the only man who does not know how to say it." This stricture, if justified, should be directed not against the language, but against its misuse. The function of a language is to express men's thoughts elegantly, accurately, and unambiguously. To achieve this end a language must be supple, adaptable, free from pedantry, and prepared to welcome immigrants. For science it must, in addition, be able to cope with the housing problem created by a rapidly expanding verbal population. Despite occasional lapses and the inevitable inclusion of technical jargon, we have forged in Lingua Medica an instrument of remarkable efficiency. It is up to us to keep it untarnished.

For the elucidation of several obscure and disputed points I have had the great advantage of consulting Dr. W. H. S. Jones, whose knowledge of Greek medical literature is encyclopaedic. I thank him most warmly.

REFERENCE

Andrews, E. (1947). *A History of Scientific English*, p. 64. New York.

AMERICAN MEDICAL ASSOCIATION

ANNUAL MEETING IN NEW YORK

The 102nd Annual Meeting of the American Medical Association was held in New York City from June 1 to 5. There were over 16,000 members present, and another 16,000 guests. At the opening session the retiring president, Dr. LOUIS H. BAUER, discussed the medico-political situation in the U.S.A. and described some of the work done for the medical profession by the A.M.A. Touching on the subject of professional ethics, Dr. Bauer said that unethical procedures must be completely stamped out. The president-elect, Dr. E. J. MCCORMICK (Toledo), in his address to the House of Delegates made suggestions towards solving some of the outstanding professional problems. "We must," he said, "be conscious of our twin roles as physicians and statesmen." Another speaker was Mrs. O. C. HOBBY, Secretary of Health, Education, and Welfare in President Eisenhower's cabinet. She stated that any Government programme of compulsory medical care would be undemocratic and uneconomic. The Government's role would be to protect public health, foster research, care for those unable to pay, and rehabilitate the disabled.

Dr. ALFRED BLALOCK, of Baltimore, well known for his contributions to the surgery of the heart, was awarded the American Medical Association's Distinguished Service Award for achievement in medicine. The award carries a gold medal and citation.

The Scientific Sections

More than 400 papers were read at the scientific sections and 21 medical films were shown. Colour television programmes, presented on screens 5 ft. by 6 ft., featured, on a closed circuit, clinical and surgical demonstrations of sinusitis, peptic ulcer, mitral stenosis, cancer of the cervix, essential hypertension, and breast tumour. A few of the papers which were read are reported below.

Cancer of the Digestive Tract

Improved methods for the early detection of cancer of the digestive tract, which is responsible for 41% of the cancer deaths in the United States each year, were demonstrated as one of the 260 scientific exhibits by a University of Chicago research team. The new method, it was asserted, has led to the diagnosis of cancer of the digestive tract with an accuracy of 90%. The technique is based on the Papanicolaou method for the early diagnosis of cancer through the recovery and identification of exfoliated cancer cells. The method, developed by Professor George N. Papanicolaou, of the Cornell University Medical College, has so far been applied most successfully in the detection of incipient cancers of the uterus and the cervix. Its application to the detection of early cancers of the digestive tract and other internal organs has proved difficult because of the difficulty of recovering exfoliated cells. The Chicago investigators believe they have succeeded in developing improved methods for the recovery of incipient cancer cells, if present, from the oesophagus, stomach, and colon, thus promising to extend the Papanicolaou technique to the early detection of the disease in those organs. A special device consisting of a balloon covered with an abrasive net, like a coarse hair-net, is inflated inside the stomach. The stomach is then washed with chymotrypsin, a natural digestive substance that dissolves the mucus in the organ's lining and frees any cells, cancerous or otherwise, that are embedded in it. This makes it possible for the abrasive surface of the balloon to gather the loosened cells for examination by the Papanicolaou method. Studies are now under way, it was learned, to determine whether a chymotrypsin "bath" may not be used by itself, without the balloon, as a satisfactory method for screening patients for possible stomach cancer. Preliminary findings were described as "encouraging." Similar methods for irrigating

and washing, it was reported, have been successful in the recovery of cells from the upper part of the colon and from the upper part of the small intestine.

Ulcerative Colitis

Drs. H. E. BACON and H. D. TRIMPI, of Philadelphia, reported a series of 302 cases of chronic ulcerative colitis treated since 1940; of these, 67 (22.4%) were operated on. Total colectomy with excision of the rectum was performed in 34 patients, and 29 of these have been completely rehabilitated. Operative mortality was nil. Five carcinomas were discovered in 5 of the 34 excised specimens: of these, four were unsuspected pre-operatively. The authors recommended a two-stage operation, the first consisting of ileostomy and colectomy, and the second of excision of the rectum. Ileostomy was not indicated unless it preceded or accompanied colectomy. In the opinion of the authors, surgery offered the removal of a precancerous bowel, a cure of the disease, and the arresting of secondary arthritic, kidney, liver, and thrombo-embolic disease.

Arterial Transfusion

Dr. SAM F. SEELEY, of Washington, D.C., spoke on arterial transfusion, saying that it had attracted wide interest in the resuscitation of patients in profound shock due to severe blood loss. He did not recommend arterial transfusion in mild or moderate shock, or even in sudden deep shock, provided adequate amounts of blood were given intravenously. In his opinion the most important contribution resulting from studies of pressure transfusions had been the recognition that even greater quantities of blood were necessary for resuscitation than was surmised even during the second world war.

Endometrial Hyperplasia and Carcinoma of the Fundus

Dr. E. R. NOVAK, of Baltimore, spoke about the relationships of endometrial hyperplasia and adenocarcinoma of the fundus. Endometrial hyperplasia was normally produced by unopposed oestrogen stimulation and could similarly be produced by exogenous oestrogens. This histological entity might be found in either pre-menopausal or post-menopausal patients, and atypical hyperactive variants occurred at any age. Hyperactive forms which were indistinguishable from true fundal adenocarcinoma might follow prolonged oestrogen therapy. Oestrogen was considered as a possible carcinogenic factor, and, since this steroid could definitely lead to extremely proliferative forms of hyperplasia, the relationship between oestrogen, hyperplasia, and adenocarcinoma had to be considered. Dr. Novak then discussed the difference between pre-menopausal and post-menopausal hyperplasia, with particular reference to its premalignant role and its treatment.

Bilateral Adrenalectomy for Severe Hypertension

Dr. R. F. BOWERS, of Memphis, reported the results of adrenalectomy in 28 patients with severe hypertension. He left a small piece of viable adrenal tissue on the left side. Pre-operative therapy with cortisone and deoxycortone acetate was given for 44 hours prior to the second-stage operation. Eight deaths occurred, all in very severe cases. The blood pressure fell to normal in all but two of the survivors, and all 20 of the survivors showed signs of mild hypoadrenalism. Maintenance dosage of cortisone ranged from nil in three cases to 60 mg. daily in one case.

The Mechanical Heart in Human Surgery

Dr. F. D. DODRILL, of Detroit, described a mechanical heart, which had been used to by-pass either the right side or left side of the human heart. The right-sided substitution was done for congenital pulmonary stenosis. A left-sided by-pass of the human heart had also been successfully carried out during the operative treatment of mitral valve disease.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Intrinsic Factor Activity in Solid Material

SIR,—Further to our article (*Journal*, February 28, p. 467) we wish to announce the isolation of a solid material with high intrinsic factor activity. In this case the source was a concentrate derived from pig gastric mucosa kindly supplied by Dr. T. Jukes of the Lederle Laboratories Division. We understand that this material produced good clinical and reticulocyte responses when given orally in a daily dosage of 40 mg., together with 10 μg. of vitamin B_{12} for ten days. Lower dosages have also been effective. The electrophoresis technique was applied to a solution of the material in buffer, and the latter was subsequently removed from the appropriate fraction. Absorption of radioactive vitamin B_{12} after oral administration was used as a test of biological activity.[1] This was carried out in collaboration with Dr. F. T. Farmer and Mr. C. Clayton.

In one patient 2 mg. of the new material produced better absorption of vitamin B_{12} than was produced by either 25 mg. or 100 mg. of the original concentrate. A second aliquot of the same concentrate fractionated in the same way yielded material which was definitely active in a dose of 4 mg. and possibly active in a dose of 2 mg. The material is homogeneous when subject to electrophoresis at *p*H 6.4, but is decomposed at *p*H 8.6 in barbitone buffer. Further evidence has been obtained that intrinsic factor is mucoprotein in nature, and most of its amino-acid and carbohydrate constituents have been identified. It is interesting to note that lysine, histidine, and tyrosine are apparently absent.

Tests are proceeding upon solid material isolated in a similar manner from human gastric juice.—We are, etc.,

A. L. LATNER.
C. C. UNGLEY.

Newcastle-upon-Tyne.

REFERENCE

Welch, A. D., *et al.* (1952). *Fed. Proc.*, **11**, 308.

Tropical Diseases in Britain

SIR,—I too have read with great interest and not a little nostalgia the annotation on this subject (*Journal*, May 16, p. 1096). I should be the first to agree with the writer upon his insistence that a microscopic examination and the discovery of malaria parasites in the blood is an essential preliminary to treatment of an attack of this fever. Early and accurate diagnosis and early and effective treatment should be the watchword for all forms of malaria; but this, alas, proves sometimes to be the counsel of perfection. As one who has seen and practised both sides from the laboratory and clinical angle for some 40 years I feel that I should qualify this statement. As Dr. W. Melville Arnott has written (*Journal*, May 30, p. 1219), the academical standpoint assumes a much more serious aspect in the case of subtertian malaria (*P. falciparum*), and it is always within the bounds of possibility that this parasite may crop up from time to time in travellers arriving by air or sea from one of the endemic areas of the disease. I can call to mind many instances where there has been no time to undertake microscopic diagnosis, and it has been necessary to act as in an emergency and inject quinine in order to save life.

I remember particularly a young man who was lying in a coma in a London hotel, having just arrived by air from South Africa. His main complaint had been acute tonsillitis, which was thought to account for the high fever, and for which appropriate treatment had been applied, when he suddenly became comatose. Intravenous quinine given without delay undoubtedly saved his life, but the diagnosis was later confirmed in the laboratory from blood films taken before quinine therapy was undertaken. One is comforted by the idea that even if the diagnosis had not been correct no real harm would have been done.

There have been others, too, in which no parasites were found in thick and thin blood films at the time of examination, but where the balance of evidence was in favour of subtertian malaria. It is undoubtedly true that occasionally, especially in the most acute and dramatic cases, the ring forms of the parasite may be particularly difficult to find in blood preparations. I have seen relapses of benign tertian malaria as well in which the same obtained but where the character of the rigor, the subsequent hot and sweating stages, and the enlarged painful spleen could leave no doubt in the clinician's mind of the correctness of the clinical diagnosis. Sometimes the discovery of malarial pigment in the mononuclear cells is confirmatory evidence.

In quartan malaria I have in mind two cases in which, although the fever and quartan periodicity were suggestive, thin blood films were searched for hours with a negative result. Finally, in one instance, however, after 2½ hours' scrutiny a single quartan parasite hove into view in a thick blood film. Intramuscular injections of quinine in these instances clinched the diagnosis by abolishing the fever when other antimalarial drugs, including mepacrine (" atebrin ") and proguanil, had failed.

The same principle similarly obtains in amoebic dysentery. It is curious that here, too, in the most acute cases with profuse diarrhoea *E. histolytica* in its active stages may be most difficult to demonstrate. I can recollect a fulminating case of this disease of an acuteness and toxicity rarely encountered, but when the proctoscope was brought into use, and scrapings made from the bleeding mucosa, these parasites were present in large numbers and the diagnosis became obvious. Another instance I can call to mind was that of an officer who when playing tennis at Wimbledon was attacked with acute diarrhoea with blood and mucus. Such was the character of the stools and the severity of the illness that he was regarded as suffering from ulcerative colitis till some three weeks later emetine was injected as an experiment and at this point the attack began to subside. Sigmoidoscopy was then performed, and active amoebae were present in the exudate in large numbers, in spite of the fact that the stools had been examined microscopically many times with a negative result. It then transpired that as a boy of 11, some 15 years previously, he had contracted amoebiasis in Mauritius.

Another difficulty crops up in intestinal amoebiasis where the lesions in the large intestine are typical of amoebic ulceration but no actual evidence of the parasite can be secured. I have had experience of many of these—some of which had been subjected to treatment for ulcerative colitis on previous occasions. Here surely is a basis for experimental therapy and for the verification of the " proof of the pudding is in the eating." If the patient recovers, and the ulcerations heal on emetine and emetine bismuthous iodide therapy, then the original clinical diagnosis must have been correct.

In these somewhat exceptional instances I am always reminded of the analogy of the rabbit. How many of us have seen their very characteristic burrows and other evidences of occupation, without obtaining so much as a glimpse of the owner, but it would be a foolish man who could swear that the occupant of the burrow is not somewhere or other ensconced inside, and this little parable is peculiarly applicable to *E. histolytica*.—I am, etc.,

London, W.1. PHILIP MANSON-BAHR.

Primary Red-cell Aplasia

SIR,—We were interested in the medical memorandum from Dr. Michael Donnelly (*Journal*, February 21, p. 439) and the letter from Drs. A. G. V. Aldridge and P. Kidd (*Journal*, March 28, p. 729) regarding cases of red-cell aplasia in infants.

We have described a case of this condition fully in a male adult African (*J. Path. Bact.*, 1953, in press). He was referred to us for anaemia, and when we saw him was gravely ill. He said he had been geting progressively weaker for about nine weeks, and complained of general body pains, weakness, and dyspnoea. His heart and lungs were normal, there was no oedema, the spleen and liver were not enlarged, there were no petechiae, there was no icterus and no sign of riboflavin deficiency. There was histamine-fast achlorhydria. He gave no history of having been exposed to toxic substances. He had been taking mepacrine, but only in the usual doses, for suspected malaria. Blood examination on admission showed: red cells 1,320,000 per c.mm.; haemoglobin 2.3 g.%; mean corpuscular volume 54 μ^3; reticulocytes nil; white blood cells 5,650 per c.mm.; platelets 700,000. A sternal puncture done on admission showed complete red-cell aplasia, with normal white and megakaryocytic elements.

He was kept under observation in hospital for eight days, during which period there was no reticulocytosis. He was then given 4 mg. daily of riboflavin for 14 days and 2 mg. daily for nine days. Seven days after the first dose of riboflavin reticulocytes began to appear in the peripheral blood (0.5%) and reached 27% on the twelfth day after the commencement of treatment. The reticulocyte response was therefore specific and reached the expected level. The red cells and haemoglobin doubled themselves in 21 days. The patient was discharged after six weeks in hospital with a blood count of 4,290,000 and 11 g.% of haemoglobin. Eight months after commencement of treatment the patient is perfectly well and has a red cell count of 5.5 million per c.mm. and a haemoglobin of 14.5 g.%. A sternal puncture done five days after the commencement of treatment showed 5% early erythroblasts, no late erythroblasts, and no normoblasts. A third marrow biopsy 12 days after the start of treatment showed 15% early erythroblasts, 27% late erythroblasts, and 34% normoblasts. Two more marrow punctures were done 23 and 30 days respectively after the commencement of treatment, and revealed that the early and late erythroblasts had decreased in number and the marrow had become predominantly normoblastic.

In view of the fact that so far all cases of true red cell aplasia have proved fatal, with the exception of one of Heilmeyer's cases and the two mentioned above, we think that our findings, if confirmed, may have a useful place in the treatment of this grave condition.—We are, etc.,

HENRY FOY.
ATHENA KONDI.

Nairobi, Kenya.

Who Was Geminus?

SIR,—To the many with a dilettantish interest in medical history the articles in your May 30 issue must have given special pleasure, although some statements may have caused surprise—for example, that the 1511 Act governing medical practice " did not apply to medical graduates of Oxford and Cambridge " (p. 1179). Were there any home-produced university medical graduates in 1511? By that date Aberdeen alone had given academic recognition to medicine, but it was merely studied as one subject in the general course, and no separate medical degrees were awarded at that time.

Some of the information about Geminus (p. 1187) seems to go further than the ascertained facts warrant. What is the evidence that he was " almost certainly a surgeon "? An individual (or individuals) with the name of Thomas Geminus (Gemynous, Gemynus, Geminie, Gemyne, etc.) is mentioned in various contemporary records—as a surgeon in the list of Edward VI's disbursements (1547-52), in the *Annals of the Royal College of Physicians* (1555), in the *Register of the Stationers' Company* (1555) as a stranger (foreigner) who was fined for calling a brother of the company a false knave and later as a benefactor to the " Brydewell," but he is not mentioned in the *Annals of the Barber Surgeons*. In addition the cognomen is associated with an excellent engraver, a printer, a cartographer, an instrument maker, and a putative author of books on anatomy. If one man possessed such widespread skill and erudition he must have been versatile indeed, and, although it is possible there was only one Geminus, an unusual name does not necessarily imply the same individual.

It is doubtful if the Geminus associated with the *Compendiosa totius Anatomie delineatio* was a medical man. Nicholas Udall in his " Address to the Reader " refers to him as a " workman," an unusual designation even in those days for a surgeon, anatomist, and author. When Vesalius complained of the plagiarism of his work by " that Englishman," he was not referring to Geminus, as your contributor infers, but almost certainly to Dr. John Caius, who had once lived and studied with Vesalius at Padua and who had returned to England in 1544, the year after the *Fabrica* and *Epitome* were first published. The Latin text used in the first two editions (1545, 1552) of the *Compendiosa* is a résumé of the *Fabrica*—it is the Vesalian *Epitome*—but in the third edition (1553), which purported to be a translation by Udall from the original Latin into English, the text actually used was a modified version of Vicary's (1548) *The Anatomie of the Bodie of Man* (itself largely pirated from de Mondeville's work), rearranged to follow the order of Mundinus's *Anathomia* (1316), which may be regarded as the first manual of practical anatomy, whereas Vesalius's *Fabrica* is a systematic treatise.

As Vicary raised no objections, while Vesalius did, we must assume that the former knew and approved of this use of his recently published work; but it is difficult to understand why the help of Nicholas Udall, *quondam* headmaster of Eton, prebendary at Windsor, and author of *Ralph Roister Doister*, was reputedly required to translate a book already in the vernacular (perhaps he translated only the plate legends which are copied

from the original Latin), or how the deception was not apparently commented upon by those familiar with Vicary's book. Caius has been blamed for instigating the plagiarism of Vesalius's great work, and it has also been suggested that Geminus is a punning pseudonym hiding the identity of Dr. Thomas Twyne, who translated other Latin works, but the association of the Vesalian plates with the Vicary script seems rather to implicate Vicary as the possible moving spirit behind this piece of artistic piracy.

There are other mysteries concerning Geminus, and not the least intriguing are how exactly his copperplates were acquired for French editions of the *Compendiosa* by Jacques Grevin, the French humanist, or how the same or similar copperplates were available for the *Anatomia Deudsch*, first published in Nuremberg in 1551, and for other German and Dutch anatomical works. Apparently Geminus had widespread connexions. Other points arise from Dr. Underwood's remarks on Geminus, and one of topical interest will be mentioned. Is the engraving on the title-page of the 1559 edition of his book a portrait of Elizabeth I? It was intended to be Queen Mary, but Queen Elizabeth had ascended the throne before the edition could be published, so the engraving (possibly with a few alterations) remained, with a fulsome dedication to the new Queen added.—I am, etc.,

Manchester. G. A. G. MITCHELL.

The Judet Operation

SIR,—Mr. T. M. Hennebry (*Journal*, May 23, p. 1166) has stated a case in favour of the Judet operation for osteo-arthritis of the hip. I would like to question some of the points he raises.

It is not reasonable to compare the results of the Judet operation for osteoarthritis with those following a fractured femoral neck. In osteoarthritis the acetabular cartilage is grossly abnormal at the time of operation. In my experience it has been unusual to find a fractured neck of femur with marked osteoarthritis. It is likely that many of the cases of fracture following the Judet operation will subsequently become osteoarthritic and painful owing to the incongruity of the surfaces. This certainly occurs after other causes of incongruity. It may, however, require a number of years for these changes to occur, and I think it is fair to say that no one yet is in a position to assess the frequency of this complication. As the majority are in the elderly, with a high mortality in the ten years after operation, it is probable that a satisfactory statistical survey on this point will take many years. This last fact justifies its use in these cases.

I would agree that many cases of osteoarthritis have a thickening of the capsule and periarticular structures which restrict movement and are certainly, in part, responsible for the pain. Your correspondent suggests that it is in this type of case with a marked contracture that the Judet operation may fail. Osteotomy in this case is almost uniformly successful in relieving the pain. This, after all, is the predominant, and often the only, complaint of the patient.

As Mr. Hennebry says in his letter, this prosthesis is "far from being the final solution." This is becoming increasingly obvious with the passage of time. His suggestion that displacement osteotomy is a retrograde step is surely a failure to recognize its indications.—I am, etc.,

Harlow Wood, Notts. J. P. JACKSON.

Treatment of Pulmonary Emphysema by Pneumoperitoneum

SIR,—We have read with particular interest the report of Drs. R. D. C. Brackenridge and A. Thelwall Jones on the treatment of pulmonary emphysema by pneumoperitoneum (*Journal*, May 23, p. 1135). For the past twelve months we have been engaged on, and have now terminated, a similar investigation on this very problem. Without wishing to anticipate the results of our report, which are now ready for publication, we wish to pass the following comments on their paper.

Vital capacity is an obsolete yardstick in the assessment of respiratory function. Three-second spirometric tests presuppose a high degree of experimental accuracy, and assume the absence of inspiratory dyspnoea.[1] Maximum breathing capacity is a much more accurate index of lung function, and there is much to commend its employment.[2] However, even here the skill, degree of experience, co-operation, and education of the patient are factors which have to be taken into consideration in the assessment of readings.

Broadly our findings are not as encouraging as those obtained by Drs. Brackenridge and Jones. Yet in a number of instances our emphysematous patients, after pneumoperitoneum, have expressed themselves as being subjectively improved in health and have stated that their dyspnoea has lessened. However, a critical evaluation of some of the variable factors involved in the assessment of dyspnoea—season, climate, intercurrent infection, bronchial spasm, and wishful thinking on the part of the patient—ought to make for the greatest caution by investigators in their interpretation of slightly beneficial or equivocal results. We feel that this view is probably true of the role of pneumoperitoneum in the assessment of pulmonary emphysema.—We are, etc.,

BERTRAM MANN.
Halifax. E. A. MURPHY.

REFERENCES

[1] Furman, R. H., and Callaway, J. J. (1950). *Dis. Chest*, **18**, 232.
[2] Donald, K. W. (1953). *British Medical Journal*, **1**, 415.

The Degradation of Flour and Bread

SIR,—I was interested to see Dr. E. H. M. Milligan's letter on the above subject (*Journal*, May 2, p. 994), for L. J. Harris[1] states that "most expert opinion now agrees that the average working-class diet in this country is so frequently low in vitamin B_1 that it would be an advantage to encourage an increased consumption of wholemeal bread." But of late there has been an increasing tendency for cases of vitamin B_2 deficiency to arise, as instanced by the frequency of beefy sore tongues and undoubted pellagrous dermatitis masquerading under the pseudonyms of neurodermatitis or even industrial dermatitis. According to Harris,[2] it is not uncommon for pellagra to occur in mental patients in this country, although it appears that the medical and nursing staffs escape this condition. It is open to question whether the hospital diet is at fault, or whether they are long-standing unrecognized cases of B_2 deficiency which had reached the last stage of all—dementia. When Sydenstricker visited this country during the late war he found a similar state of affairs. The fact that, despite the so-called restoration of flour, cases of nicotinamide deficiency do arise makes one ponder that all is not well; and it appears that matters will worsen when the extraction rate of flour is again raised. Furthermore, cases of acute encephalopathy and confusional insanity are known to arise, especially in the elderly, after severe operations such as hysterectomy or prostatectomy, which are similar in most respects to delirium tremens and curable with adequate doses of nicotinamide.—I am, etc.,

Heanor, Derbyshire. PHILIP TURTON.

REFERENCES

[1] *Vitamins and Vitamin Deficiencies*, 1938, vol. 1, p. 137. J. and A. Churchill, London.
[2] *Vitamins, A Digest of Current Knowledge*, 1951. J. and A. Churchill, London.

Antabuse Addiction

SIR,—All those who deal with alcoholics have observed the variability of the antabuse-alcohol reaction in different subjects. This variability is to be expected, for the aversion effect of antabuse therapy does not depend on the physical symptoms when alcohol is taken—the vasodilatation, headache, tachycardia, and nausea—but on the concurrent subjective state of the patient. This is a feeling of impending personal catastrophe which, like tolerance of pain, varies from subject to subject. A great many psychopathic drinkers show a magnificent tolerance for acetaldehyde, and considerable bravado. They often claim that a small gin

makes them feel like several doubles when on antabuse. It is noticeable, however, that they prefer to omit their antabuse. The more labile psychoneurotic is often profoundly disturbed by the antabuse-alcohol reaction and avoids alcohol.

A small group of patients has emerged, however, who, in spite of recurrent terrifying experiences with the reaction, repeatedly ask to be put back on antabuse. Their assertion that they are now certain that this will stop their drinking appears to be a rationalization, for in a short time they proceed to drink again, even carrying antabuse tablets with them in some cases and swallowing more of them whilst drinking. These patients obviously tend to become rapidly confused, restless, and uncoordinated whilst indulging in this procedure. They also seem to show an increased tendency to self-reproach when sober. Can it be that these patients incorporate antabuse into their drinking pattern not only to achieve more rapid escape from insupportable tension but also to inflict simultaneously the punishment demanded by a harsh super-ego which is, of course, part of that tension ?

However this may be, these patients show the surprising tendency to seek antabuse as an adjunct to their drinking, and they thus appear to be unsuitable cases for treatment with the drug.—I am, etc.,

Twyford. L. C. F. CHEVENS.

Smoking and Cancer of the Lung

SIR,—Mr. P. G. Moore's letter (*Journal*, June 6, p. 1281) obscures very nicely the point which we wish to make (*Journal*, May 16, p. 1105), and is far from giving the precision he suggests. Diphtheria has been virtually wiped out as a cause of death in this country. This has had very little effect on the expectation of life, because the large number of children who never had the disease are included in this figure. But the chance of dying between the ages of 1 and 15 has been materially decreased, because diphtheria used to cause a considerable proportion of deaths between these ages. In exactly the same way, even if lung cancer were abolished, the expectation of life would not be changed very much, but the chance of dying in middle age would, because lung cancer is an important cause of death at this age.

The expectation of life, or mean future life time, at any age, if considered by itself, has the same limitation as any other mean value in that it gives no information concerning the shape of the distribution from which it is calculated. It is for this reason that it is rarely used by actuaries in the comparison of mortality. Mr. Moore's figures, if taken in conjunction with those in our letter, will serve a most useful purpose in providing a practical demonstration that an apparently small difference in the expectation of life may conceal a substantial difference in mortality.—We are, etc.,

London, N.W.10. J. A. HEADY.
London, W.1. R. G. BARLEY.

Limb Injuries in Coal-miners

SIR,—Dr. C. T. H. Whiteside in his letter (*Journal*, May 30, p. 1222) remarks that it would be interesting to know if the high percentage of limb injuries which he found in a colliery in Kent is representative of the country's coal-mines as a whole. A very detailed accident analysis is made by the South Western Division of the National Coal Board and figures showing the part of the body injured can be extracted. In the year 1951, among a population of 106,000 miners, injuries to the limbs accounted for 61% of all injuries causing absence of more than three days' duration (upper limb 36%, lower limb 25%). These figures support Mr. Whiteside's contention that limb injuries constitute the greater proportion of all injuries sustained in the coal-mines. The analogy which he draws between war, in which about 50% of the total injuries are limb injuries, and coal-mining is not in my opinion particularly appropriate. If a little thought be given to the nature of coal-mining operations it will not seem so surprising that limb injuries are predominant. A more appropriate analogy might be the proportion of limb injuries in heavy industry other than coal-mining.

Dr. Whiteside's estimate that there are about 250,000 accidents per year, each causing absence of more than three days, among the total mining population is fairly accurate, and it is undeniable that this is a startling and appalling figure. It should be borne in mind, however, that this figure may be swollen by changes in the law relating to compensation and that the fatal accident rate, which cannot be thus affected, has been falling steadily for many years. The number of fatal accidents between 1922 and 1940 remained around or above 0.40 per 100,000 man shifts worked. After a rise in 1941 and 1942 the rate declined more or less steadily to 0.25 in 1948 and 1949, the 1952 figure being 0.23.

The mining industry is well aware of the seriousness of the accident problem, and is systematically attacking it in a number of different ways. The industry is also fully seized of the necessity for active research, and the N.C.B. are at present supporting two research projects which have the aim of, *inter alia*, defining the causes of accidents in all their technical detail. In these investigations the importance of limb injuries, which Dr. Whiteside has emphasized, will not be overlooked.—I am, etc.,

Medical Service, National Coal Board, London, S.W.1. J. S. MCLINTOCK.

Transverse Arrest of Head

SIR,—May I refer to some of the points raised in the discussion on transverse arrest of the head ? When I wrote my article (*Journal*, April 18, p. 865) I was not aware of the teaching of Mr. Wilfred Shaw on this subject, and I regret, therefore, that I did not refer to the very clear account of this complication which he gave in 1933.[1] Also the monograph by Mr. Parry Jones on the Kielland forceps[2] had not yet appeared. This important work is a credit to British obstetrics, and should be studied by all who use or intend to use this instrument.

Much of the discussion has centred around the use of the Kielland forceps, and there is now general recognition of its value. Its introduction has constituted, I believe, a big obstetrical advance, not because it possesses any inherent magical properties, but because its use demands a careful study of each case and a proper cephalic application. Mr. Parry Jones in his letter (*Journal*, June 6, p. 1278) has drawn attention to the important point that the "wandering method" of application is almost as classical as the one involving rotation of the anterior blade.

I did not intend to give the impression, as Mr. A. P. Bentall suggests (*Journal*, May 16, p. 1107), that cases of transverse arrest can only be dealt with by those who have mastered the use of this instrument, nor did I intend, as Mr. Rutherford Morison fears (*Journal*, May 16, p. 1107), to exclude the general-practitioner obstetrician from using this instrument. I believe, however, that all who may be up against this complication will be the better able to deal with it if they have studied the technique of using the Kielland forceps. Mr. Bentall disagrees with my statement that deep general anaesthesia is necessary for manual rotation. He admits, however, the necessity for rotation of the shoulders with this manœuvre, and Munro Kerr and Chassar Moir[3] refer to the need for "deep surgical anaesthesia."

Dr. J. D. Martin (*Journal*, May 16, p. 1107) himself admits the difficulty of comparing the various figures for the foetal risk for the various methods of instrumental delivery in the true occipito-posterior positions. I feel, however, that my figures showing only one foetal death in 55 primigravidae delivered in the face-to-pubes position with forceps justify the claim that this method of delivery has a low foetal risk. Admittedly with this technique the strain on the soft tissues is great, and the risk of severe lacerations in unskilled hands is high. Manual or forceps rotation, however, is also not free from serious risk in this respect.—I am, etc.,

Middlesbrough. BRYAN WILLIAMS.

REFERENCES

1 *Practitioner*, 1933, **131**, 685.
2 *Kielland's Forceps*, 1952, Butterworth and Co. (Publishers), Ltd., London.
3 *Operative Obstetrics*, 1949, 5th ed., p. 131, Baillière, Tindall and Cox, London.

Obituary

S. A. WINSTANLEY, M.B., Ch.B.

We record with regret the death on June 1 of Dr. S. A. Winstanley. The announcement of his death to the Annual Conference of Local Medical Committees last week evoked an expression of very real regret at the passing of a long-familiar figure and an old friend and counsellor. For more than a quarter of a century Winstanley had always been in the Lancastrian group at such Conferences, and though he was not a frequent speaker, either there or in the Representative Body, and certainly claimed no gift of oratory, his advice, modestly proffered, was highly valued, if not always followed. The place in which he excelled was the committee, and not many men have a longer record of committee work on behalf of the Association. His membership of the Insurance Acts Committee and its successor, the General Medical Services Committee, lasted unbroken for nearly a quarter of a century, and was relinquished only a couple of years ago.

Sydney Adams Winstanley was a Lancashire man by birth and education. His whole career was spent within a few miles of Manchester City Hall. He was born at Pendleton by Salford on November 25, 1878, and was educated at Manchester Grammar School, from which he went on to Victoria University, graduating M.B., Ch.B. in 1914. After acting as house-surgeon at St. Mary's Hospital, Manchester, he settled in general practice at Urmston, a town a few miles to the south-west of Manchester. He was from an early stage in his career what would now be called a general-practitioner specialist, his interest being in obstetrics. As long ago as 1922 he published in the *British Medical Journal* notes on 259 cases of labour conducted by "twilight sleep," a subject which at that time was arousing particular interest. A few years later Winstanley served on a subcommittee of the British Medical Association set up to report on the general question of anaesthetics in midwifery. But he was a typical general practitioner, if such a being exists, much liked by his patients and colleagues. Among other appointments he held was that of medical officer to the Urmston Cottage Hospital.

Joining the British Medical Association in 1919, Winstanley soon began to take a part in local and eventually in central affairs. His first official appearance at Headquarters appears to have been as a newly elected member of the Insurance Acts Committee in 1928. For some years he was a member of the executive of that body, also of the negotiating committee which was formed in 1944 and continued until after the National Health Service was well established. He was a member of the Medical Planning Commission set up in 1940, for ten years a member of the Services Committee, for four years a member of the Association committee concerned with the problems of demobilization, and from 1938 to 1951 a member of the Central Medical War Committee. His help seems to have been sought in all the various problems of the National Health Insurance service—remuneration, regulations, prescribing, additional benefits, organization of public medical services, and so on. There were subcommittees set up at various times to deal with these matters and Winstanley was a member of them all. He served also on the Spens Committee set up in 1945, which had its repercussion in the Danckwerts award. Like so many Lancastrians, Winstanley had a highly developed business sense. National Health Insurance practice, he once said, was never at any time a sound business proposition, except in so far as it was subsidized by private practice, and he foresaw, several years before the advent of the National Health Service, that this "subsidy" would diminish in value. In 1942 he moved to instruct the Insurance Acts Committee to apply for a wartime capitation fee of fourteen shillings, and, failing satisfaction, to call upon practitioners to give the requisite notice of withdrawal of service, adding, however, that this action did not imply a strike, because the insured population would obtain their attendance by the application of the "own arrangements" clause. He failed to carry the Conference with him.

In his own Manchester area Winstanley was prominent in medico-political affairs—a member for many years, and eventually chairman, of the Local Medical and Panel Committee for Lancashire, chairman of the Manchester Division in 1935–6 and again from 1946 to 1950, and year by year he was sent up to the Representative Meetings. He was also a member of the Manchester Medical Society and of the North of England Obstetrical and Gynaecological Society. He was a man eager to serve his profession, as was shown by the mass of varied committee work he undertook, but there was about him a certain shyness which accounted for the fewness and brevity of his interventions in debate. His alert and likeable personality will be greatly missed.

Dr. ARTHUR B. MCMASTER, formerly medical officer of health for Dover, died at his home at Dover on May 25, in his 79th year, after a long illness. Arthur Berry McMaster was a native of Athlone, the posthumous son of a clergyman. By means of scholarships and exhibitions he was able to pay for most of his education. At Queen's University, Belfast, he was a distinguished student, taking many prizes, including the Gold Medal for Midwifery. He qualified M.B., B.Ch., B.A.O. in 1898, and proceeded M.D. in 1902. For some years McMaster was in general practice, first at Rochdale and later at Stockport. But his health was never robust, and in 1909 on medical advice he gave up general practice. After taking the D.P.H. at Manchester he specialized in public health, holding his first appointment at Crewe. In 1920 he was appointed M.O.H. and port medical officer, Dover. Here he reorganized to a high pitch of efficiency the public health department and port medical service. He retired in 1939, but continued for the duration of the war as M.O.H. for the Borough of Sandwich and East Kent No. 2 District. For over 50 years he was an active member of the British Medical Association, being chairman of the Dover Division from 1927 to 1929, and president of the Kent Branch in 1929. He was also deeply interested in the work of the St. John Ambulance Brigade, and was an assistant district commissioner. As a man McMaster was quiet and reserved. Apart from his profession, his chief interests were in reading and his garden; he played an active part in parish affairs, and was churchwarden for many years. Dr. McMaster was twice married, and leaves a widow and two sons.

We record with regret the death of Dr. DAVID GAMBLE MADILL on May 27 at his home at Sutton, Co. Dublin. The son of a Presbyterian minister at Garvagh, Co. Armagh, Madill was educated at Coleraine Academical Institute and Trinity College, Dublin, where he graduated M.B., Ch.B., B.A.O. in 1908. Whilst he was a student at Dublin he obtained the Haughton Medal and the Surgical Travelling Prize. After qualifying he became a house-surgeon at Sir Patrick Dun's Hospital, and later became assistant to Dr. Henry Jellett there. Madill subsequently became assistant

master of the Rotunda Hospital. In 1929 he became a founder Fellow of the Royal College of Obstetricians and Gynaecologists.

We are indebted to B. S. for the following appreciation: David Madill was one of my greatest friends in Trinity College, Dublin, where he was a medical student in the year junior to mine. He had entered the University before me, but had decided to take a special degree in experimental science, and succeeded in obtaining a first-class moderatorship. After he entered the medical school he was a very successful coach for students competing for the examinations in botany and zoology. He joined Sir Patrick Dun's Hospital, where later he became house-surgeon, and this post was followed by his appointment there as assistant to Dr. Henry Jellett. When Dr. Jellett became Master of the Rotunda Hospital he nominated Madill as his assistant. This proved to be a first-class choice. He was an excellent teacher and operator, and was very popular with post-graduates, students, and nurses. A couple of years after he had completed his time as assistant master he was appointed gynaecologist to the Adelaide Hospital, where he continued his successful career. He was also gynaecologist to Monkstown Hospital. He acquired a large practice and was beloved by his patients. Madill did not publish a great deal, but he acted as co-author in Dr. Jellett's widely read large textbook on midwifery. Unfortunately, Madill was bedridden in his last two or three years. He married Miss Georgina Lauder, of Sutton, who was one of the most popular figures in Ireland and who was in the championship class in golf. Madill himself took up the game, but never achieved distinction. They had one daughter, and to his wife, daughter, and grandchild we extend our heartfelt sympathy.

Dr. JOSEPH R. MUTCH died at his home in Aberdeen on June 2 at the age of 58. His illness and death came as a profound shock to his many friends, colleagues, and patients, as until a few weeks before his death he was apparently in good health. Joseph Raeburn Mutch was a native of Cornhill, Banffshire. He was one of a large family, and like so many successful doctors his upbringing was humble. Opportunities were not presented to him, but he was endowed with a high intelligence and a tremendous capacity for hard work. He was dux of the village school, but was unable to continue his education. He became apprenticed to a watchmaker. During this time he developed a disease of his hip-joint which incapacitated him for two years and left him with a limp. However, during the 1914–18 war he served in the Gordon Highlanders as a clerk, and in the Royal Flying Corps as an instrument-maker. After the war Mutch opened a business in Aberdeen as a watchmaker. He then proceeded to qualify as an optician; but this did not satisfy him, and only stimulated him to higher endeavour. He began to study medicine at the University of Aberdeen when he was 34. He graduated M.B., Ch.B. in 1934. The following year he passed D.O.M.S.Eng., and in 1936 he proceeded M.D. Mutch's one consuming interest was the eye, and it is small wonder that he devoted his professional life to it. He was soon appointed to the staff of the Aberdeen Royal Infirmary. He carried on a large private practice, but on the introduction of the National Health Service he became a full-time consulting ophthalmologist to the North-Eastern Regional Hospital Board. His professional life was short, but he accomplished what many would consider a lifetime's work: he published many papers and did much original research. He was particularly interested in the effect of diet on the eyes. He had many outside interests: he made a collection of barometers, clocks, and spectacles; he loved gardening and photography; he was an active member of the B.M.A.; and he was an elder of the kirk and a keen Rotarian. Success left Joseph Mutch unspoiled. His struggle did not harden his heart, but gave him a sense of real values. He could not tolerate sham or humbug. In spite of his somewhat gruff approach he was the gentlest of men. The world is the richer for his living, and he will be missed.—C. B. G.

We are indebted to Dr. FRANK COLEMAN for this appreciation of Dr. ALFRED NOLAN FELL, whose death was recorded in the *Journal* of May 23 (p. 1169): As a school-friend of Nolan Fell I should like to express my appreciation of his sterling qualities and integrity of character. I knew him in the 'eighties while we were together at Nelson College, New Zealand. He played cricket and Rugby football for the college for three years. Whilst at Otago University he was considered the best attacking three-quarter in the colony of New Zealand. At Edinburgh in 1901 he captained the university fifteen during their phenomenal year when they played sixteen matches without a loss, and he subsequently played for Scotland against England, Wales, and Ireland. He won the Muir Cup at Edinburgh University in 1900, and in the same year obtained a double blue. Fell's academic record was almost as brilliant. Whilst in practice at Colchester yachting was one of his favourite pastimes, no doubt acquired from his father's love of this sport in the harbour of Nelson.

Medical Notes in Parliament

DEATH OF A SOLDIER

Wing Commander N. J. HULBERT on June 16 asked the Secretary of State for War if inquiries were completed in regard to the death of Private Donald Harrison, of Stockport, who died in Moston Hall Military Hospital in April.

Mr. ANTHONY HEAD in reply said that Private Harrison, aged 18, was called up for military service in January, 1953, when he was passed as medically fit. On March 13 at Wrexham he reported sick with a pain in his back, which the medical officer in charge of his unit diagnosed as fibrositis. He again reported sick on March 26, when the medical officer diagnosed "Query hysteria" and ordered his admission on March 26 to the Military Hospital at Chester. On admission he was given by the admitting medical officer a preliminary medical examination, which included a detailed examination of the central nervous system, for the purpose of allotting him to the appropriate medical division of the hospital. The admitting officer made a firm but not final diagnosis of hysteria. This preliminary examination was correct in so far as Harrison was undoubtedly suffering from hysteria. The fact that it was not discovered that he was also suffering from a rare and malignant disease was not necessarily at this stage due to negligence, since a more detailed subsequent examination should have taken place after admission to the ward.

After admission Private Harrison was required by the medical staff of the hospital to fend for himself, and other patients were forbidden to help him. The treatment of hysterical patients did require that they should be encouraged to help themselves, but in no circumstances should it entail harshness. Although he complained that he could not use his legs, he was left to get about as best he could by himself. This treatment continued for five days, during which time Harrison's condition deteriorated, and he (Mr. Head) was satisfied that the continuance of this type of treatment was due to negligence and undoubtedly resulted in harshness. A full physical examination was always required before a diagnosis of hysteria could be justified, and should have been made on the first day in the ward. The medical specialist looking after Harrison should have satisfied himself that this had been done. This he neglected to do. Furthermore, although during these five days Harrison frequently complained of pain in his legs, thighs, and back, and although this was recorded by the subordinate nursing staff, the day sister in charge of the ward never drew the attention of the medical specialist to Harrison's repeated complaints. This wrong and harsh treatment was continued despite the comments and protests of at least one other patient in the ward.

It was not until Tuesday, March 31, that Harrison was seen by a psychiatrist and thereafter received sympathetic

handling, but even at this stage a full examination had not been made.

On the night of April 1 the medical orderly became worried about Harrison's condition and called the orderly medical officer, and then for the first time Harrison was given a full medical examination. The orderly medical officer realized at once that Harrison was dangerously ill, and from this time he was treated for the malignant disease from which he was suffering. Harrison died early on the morning of April 5.

Irregularities and Mistakes

At the time of his admission to hospital Harrison's illness had undoubtedly reached a stage when death was inevitable, since malignant disease of this type in youth, though rare, grew very rapidly. He (Mr. Head) did not suggest that this in any way excused the mistakes made in the handling of the case.

After Harrison's death it should have been abundantly clear to the commanding officer of the hospital that serious irregularities and mistakes had occurred. Yet, so far as he could ascertain, no thorough inquiry was instituted by the commanding officer, although on May 18 he stated that a full inquiry had already been made by himself and that he was satisfied that there was no truth in the allegations that there had been ill-treatment of patients.

This serious occurrence was caused not by any fault in the method of procedure laid down for Army hospitals but by the failure of certain individuals to carry out their duties. The commanding officer would be called to account for his conduct and be tried by court-martial. The medical specialist concerned, who left the R.A.M.C. in May, would be reported to the General Medical Council. The day sister concerned, who was a civilian, had had her contract terminated and would be reported to the General Nursing Council.

Nurses Sensitive to Penicillin

Asked on June 18 what number of district nurses had developed a sensitivity to penicillin and could not undertake further nursing duties, Mr. IAIN MACLEOD said the total number of district nurses affected was not known, but a special inquiry had shown that in 70 local health authority areas 73 nurses had become sensitive to penicillin and had to give up nursing for varying periods. There was evidence that the incidence could be reduced by strict observance of technical precautions. He had at once obtained advice on this from his Standing Medical Advisory Committee and was circulating this advice urgently to local health authorities and others concerned. Mr. Macleod further said that nurses who had to give up work by reason of sensitivity to antibiotics were entitled to the normal sick-leave allowances and could, in appropriate cases, qualify for incapacity benefit under the National Health Service (Superannuation) Regulations. They might also, when the circumstances warranted it, qualify for industrial injuries benefit. The numbers, if any, who might have to give up nursing permanently were not yet known.

Casualties in Korea.—United Kingdom casualties in Korea between July 1, 1951, and June 1, 1953, were 2,237 officers and men, of whom 447 were killed or died of wounds. For the same period, total United Nations casualties, including South Korean and United Kingdom casualties, were about 180,000, of whom about 35,000 were killed.

Coronary Thrombosis.—On the advice of the Advisory Committee for Medical Research in Scotland, five grants from National Health Service funds have been made for research on coronary thrombosis. At March 31, 1953, £5,100 had been paid, and £11,600 remained to be paid during this year.

Chalk in Flour.—In the 12 months ending May 23, 1953, 11,369 tons of calcium carbonate were added to national flour. The whole of the supplies conformed to the specifications of the *British Pharmacopoeia* and were obtained from home sources.

Physiotherapists.—There were 4,178 physiotherapists employed in hospitals in the National Health Service in England and Wales on December 31, 1952 ; 3,250 were full-time and 928 part-time.

Universities and Colleges

UNIVERSITY OF EDINBURGH

The Queen has appointed Dr. D. J. A. Kerr, Lecturer in Forensic Medicine at Edinburgh University, to be Regius Professor of Forensic Medicine, in succession to Sir Sydney Smith, who is resigning on September 30, 1953.

UNIVERSITY OF LONDON

Miles Weatherall, D.M., Senior Lecturer in Pharmacology at London Hospital Medical College, has been appointed to the University Readership in Pharmacology tenable at that College.

L. F. Lamerton, M.Sc., Ph.D., Senior Assistant Physicist at the Royal Cancer Hospital, has been appointed to the Readership in Physics applied to Medicine tenable at the Institute of Cancer Research, Royal Cancer Hospital.

Dr. A. d'A. Bellairs, Lecturer in Anatomy in the University of Cambridge, has been appointed to the Readership in Anatomy, tenable at St. Mary's Hospital Medical School.

Dr. K. W. Cross, Senior Lecturer in Human Physiology at St. Mary's Hospital Medical School, has been appointed to the Readership in Human Physiology tenable at the school.

The title of Reader in Anatomy in the University has been conferred on Dr. J. T. Aitken in respect of the post held by him at University College.

Donald Arthur McDonald, D.M., Senior Lecturer in Physiology at St. Bartholomew's Hospital Medical College, has been appointed to the University Readership in Physiology tenable at the College.

W. C. J. Ross, Ph.D., D.Sc., has been appointed to the Readership in Chemistry tenable at the Institute of Cancer Research (Royal Cancer Hospital), from January 1.

Dr. D. Robertson Smith has been appointed Lecturer in Clinical Pathology in King's College Hospital Medical School and Honorary Assistant Clinical Pathologist to the hospital, and Dr. D. G. Rushton Junior Lecturer in Morbid Anatomy in the Medical School.

Mr. L. H. Savin, senior ophthalmic surgeon at King's College Hospital and the Royal Eye Hospital, has been appointed a Fellow of King's College, and Professor R. Milnes Walker, professor of surgery in the University of Bristol, a Fellow of University College.

The following scholarships at the Royal Free Hospital School of Medicine have been awarded for 1953–4: *A. M. Bird Entrance Scholarship*, Miss G. Freeman (City of London School for Girls); *Mrs. George M. Smith Scholarship for Women*, Miss M. L. Shaw (Pontefract and District Girls High School); *MacIntyre Evans Scholarship for Women*, Miss G. R. Perry (Royal Free Hospital School of Medicine); *Elizabeth Garrett Anderson Scholarship for Women*, Miss D. I. Hawkins (Royal Free Hospital School of Medicine); *Dr. Margaret Todd Scholarship for Women*, Miss R. D. Low (Royal Free Hospital School of Medicine); *A. M. Bird Scholarship for Clinical Studies*, Miss A. M. Horn (Royal Free Hospital School of Medicine).

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examination indicated:

ACADEMIC POSTGRADUATE CERTIFICATE IN PUBLIC HEALTH.—J. Carlton, G. J. Glynn, Winifred M. Hiscock, K. A. Rahman, S. Sandmo, D. Ungar, D. Yarom.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

PH.D.—*In the Faculty of Medicine:* E. S. Jones.

FINAL M.B., CH.B.—*Part II:* J. D. Agnew, J. A. Barlow, A. G. Bowers, M. J. A. Britten, N. T. Burnett, B. J. Charlick, R. W. Coffee, J. S. Comaish, J. R. Cope, G. W. Danger, K. S. Davies, R. J. G. Downie, Florence M. Dukenfield, D. P. Duffield, T. R. Evans, R. Finn, J. G. Foley, D. Gardner, Anne M. Godfrey, D. H. Goldsmith, Mary Gregson, Patricia O. Grundy, W. B. Hanley, P. A. Harrison, J. W. Hill, H. B. Hilton, E. J. M. Hopkins, C. L. Imison, R. A. Johnson, P. L. Jones, P. King, J. B. Laine, V. Leach, C. L. Levene, G. Lloyd, B. A. Lowe, Joan K. McCann, Anne D. Micah, J. B. Middleton, J. M. Nichols, F. T. O'Brien, B. J. O'Dowd, L. Ratoff, M. R. Rayman, A. Roberts, S. S. Rubenstein, M. J. Samuels, H. Savage, Eleanor K. Scott, T. F. Shelley, Mary E. Shepherd, A. Speakman, D. Taylor-Robinson, D. A. Thomas, R. S. Todd, V. Tonge, A.

Turner, M. R. B. Wallice, W. P. Walsh, P. K. Wilson, Elizabeth A. Witham, N. C. Woodier, G. H. Worsley, I. Wort.

DIPLOMA IN PUBLIC HEALTH.—*Part I:* C. Sudhipongse.

DIPLOMA IN RADIOLOGY.—*Radiodiagnosis, Part I:* B. K. Bajaj, W. C. Heron, P. McCann, P. N. Newsam. *Radiotherapy, Part I:* H. J. J. Beyleveld.

D.T.M.&H.—K. M. Aboud, A. N. Basu, S. N. Bhattacharya, K. R. I. Hariharan, R. Hecker (recommended for the award of the Milne Medal in Tropical Medicine and the Warrington Yorke Medal in Tropical Hygiene), E. S. Jones, G. Moles, Y. Na Songkhla, H. C. C. Nwankwo, T. Viriyakul.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a quarterly meeting of the College held on May 5, with the President, Dr. W. A. Alexander, in the chair, the following were elected Members of the College: D. S. Nand, G. R. B. Kumarakulasinghe, W. MacLeod, S. N. Wanchoo, L. K. Ganguli, W. D. L. Fernando, N. Y. McCallum, E. W. Moore, M. Hasan, R. A. Gulmohamed, I. F. Sutherland, D. A. I. Grewar, B. Senior, N. Feldman, Y. Ho, Q. G. Quah, S. K. Biswas, W. S. A. Allan, T. H. Maniar, K. Z. Hasan, M. M. Baig, W. L. F. Hatchuel, A. Sandler, I. N. Marks, A. T. Lambie, J. K. McKechnie, C. Nwokolo.

The College approved of regulations permitting suitably qualified persons to read in and borrow from the library. The College library, the use of which has hitherto been restricted to Fellows, was founded in 1681 and is the oldest medical library in Scotland. It is almost entirely restricted to medicine and contains nearly 200,000 volumes.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on May 20, with Professor Walter Mercer, President, in the chair, the following candidates, having passed the requisite examinations, were admitted Fellows: A. J. C. Allison, A. E. Amoils, E. S. Chellappa, A. F. G. C. Christie, D. C. Cooke, E. C. Edwards, J. C. Foster, J. D. Fraser, D. R. Gunn, I. A. Harris, H. H. Martin, J. S. Mehta, M. N. Menzies, L. L. Ptak, K. Rubinstein, U. N. Shahi, M. R. Shirazi, J. D. C. Sim, I. M. Stewart, G. G. Vashi, R. D. Venn, W. F. Walker, I. Wilson.

SOCIETY OF APOTHECARIES OF LONDON

The diploma of L.M.S.S.A. has been granted by examination to the following successful candidates: G. Hamlet, J. V. Parson, A. McL. Keil, J. S. Bennett, P. M. Teng, N. Kaan, W. J. G. Hughes, F. L. D. Steel, C. E. Lay.

The following candidates have been awarded the Diploma in Industrial Health: M. S. Bopari, P. K. Bose, J. Fairlee, A. Munn, P. N. B. Peacock, S. Mukherjee, W. E. Scott, D. K. Ramadwar.

Mr. E. J. Dearman, Bedel of the Society, retired on February 28, after 52 years' service with the Society.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examination, were admitted L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.&S.G., on March 7: I. D. Archibald, B. R. Bayne, I. C. Beard, S. C. Bose, S. Burton, Lydia F. G. Cowan, J. A. W. Dressler, Catherine B. Gregor, L. A. Harris, M. L. M. Izzadeen, C. R. Lee, W. T. M. MacNeish, D. N. Randeria, R. H. Rosen, M. R. Soliman, Sheila C. Spark, D. C. Stevenson, Margaret J. Taylor, J. R. Ward, G. J. Whiston.

CONJOINT BOARD IN IRELAND

The following candidates were successful in the Spring post-graduate examinations:

DIPLOMA IN OPHTHALMIC MEDICINE AND SURGERY.—G. E. C. Hewson.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—S. Lennon, D. E. Munro, E. O. Lundholm, B. G. Fleming, C. McP. Smith, M. A. Rahill, J. W. Sandler, R. A. Robinson, B. A. O'Connell, D. H. A. Irwin.

DIPLOMA IN CHILD HEALTH.—G. Bheek, F. P. S. le Roux, Margaret Magill, A. J. MacDonald, A. J. Edwards, E.O'Connor, T. D. Shanahan.

The following candidates were duly admitted licentiates in medicine and midwifery on March 27, having passed the final examination in medicine, surgery, and midwifery of the Conjoint Board of Ireland: J. M. Anklesaria, C. P. Carey, T. H. Chillingworth, J. A. Davies, I. H. C. Lynch, E. A. Moore, I. Parbhoo, W. V. Reynolds, D. Ryan, J. F. L. Watson.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 6** (No. 22) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	10	2	3	0		24	1	11	1	1
Dysentery	397	68	70	3	1	276	25	84	4	1
Encephalitis, acute	5	1	0	0		3	1	0	0	
Enteric fever:										
Typhoid	0	0	0	0		3	0	0	0	
Paratyphoid	6	0	1 (B)	1		45	0	12 (B)	0	
Food-poisoning	204	33		1		137	11		3	
Infective enteritis or diarrhoea under 2 years				18	24				13	24
Measles*	8,726	297	308	234	252	6,616	519	376	219	386
Meningococcal infection	25	1	16	1	3	31	2	12	3	1
Ophthalmia neonatorum	25	0	9	0		39	5	13	0	1
Pneumonia†	317	14	140	5		380	20	165	7	
Poliomyelitis, acute:										
Paralytic	36	1	3	0	2	26	2	2	0	2
Non-paralytic	15	0				18	0			
Puerperal fever§	174	25	16	0		225	25	11	1	2
Scarlet fever	758	37	141	36	40	915	69	165	16	43
Tuberculosis:										
Respiratory			147	19				175	26	
Non-respiratory			23	5				23	6	
Whooping-cough	2,371	178	341	36	80	2,595	125	175	81	118

DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0	0	0		0	0	0		0	0
Dysentery	0	0				0	0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0			0	0		0	
Infective enteritis or diarrhoea under 2 years	10		3	3	0	11		4	1	0
Influenza	3	0	0	0	0	5	1	3	1	0
Measles		0	1		0		0		0	0
Meningococcal infection		1	0				0			
Pneumonia	125	11	9	8	5	139	14		9	3
Poliomyelitis, acute	1	0			0	1	0			0
Scarlet fever		0	0		0		0		0	0
Tuberculosis:										
Respiratory	74	10	10	0	5	87	10	13	2	8
Non-respiratory		0	2	0	1		0	2	1	0
Whooping-cough	1	0	1	0	0	1	0		0	0
Deaths 0–1 year	212	26	14	10	13	203	21	30	9	13
Deaths (excluding stillbirths)	4,317	608	452	92	115	4,479	625	539	98	148
LIVE BIRTHS	7,759	1052	927	232	417	7,758	1149	919	216	427
STILLBIRTHS	178	25	30			201	35	21		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Food-poisoning in Lancashire

Over 1,000 persons are believed to have suffered from food-poisoning last week in an epidemic which affected a number of towns (including Preston and Blackpool) and sanitary districts in north-west Lancashire. For the following information we are indebted to Dr. A. Dodd, divisional medical officer of health, Division No. 3 of the Lancashire county administrative area.

During the period June 13 to 20, 135 cases of food-poisoning were notified from 6 of the sanitary districts in the division. In addition 129 cases were known but not notified, giving a total of 264 cases. Three county boroughs and other districts of the administrative county were affected, some earlier and more severely than No. 3 Division. The vehicle of infection is believed to have been a large batch of meat pies manufactured on June 10 and 11. It may be that some pies baked on June 9 and 12 were also infected. A report on the morning of June 13 of the occurrence of two cases of food-poisoning and the information that meat pies, among other foods which had been eaten, resulted in a decision the same morning to stop production of meat pies. Staff at the place of manufacture were interviewed, excluded from work when justified by circumstances, and faecal specimens submitted for investigation. Distribution lists of meat pies were passed to appropriate local authorities in order that unsold meat pies could be destroyed or subjected to laboratory test and consumers traced if possible.

Salmonella morbificans bovis was isolated from faeces of persons affected and from meat pies. No pathogenic organisms were isolated from powdered gelatin, flour, fat, or a first sample of the main carcass meat used in the manufacture of pies. It was not possible to obtain meat from each source for test. Salmonella organisms were isolated from several persons employed at the bakery who were probably infected by eating meat pies, but the finding in one case may prove to be significant. Investigations continue, particularly concerning meat supplies.

Clinical reports show that the incubation period varied from 6 to 30 hours, usually about 18 to 24 hours. Shivering or abdominal colic or vomiting (sometimes very severe) was followed by diarrhoea, accompanied by headache, pains in the limbs, and general prostration. The duration of illness was from eight hours to five days. The severity of symptoms was very variable. At the time of writing these notes only two persons are known to have been admitted to hospital from No. 3 Division of the Lancashire county administrative area, but it is understood that more were admitted to hospital from other districts, and that two deaths may have been due to the infection. Primary cases are still being reported, and also a few secondary cases.

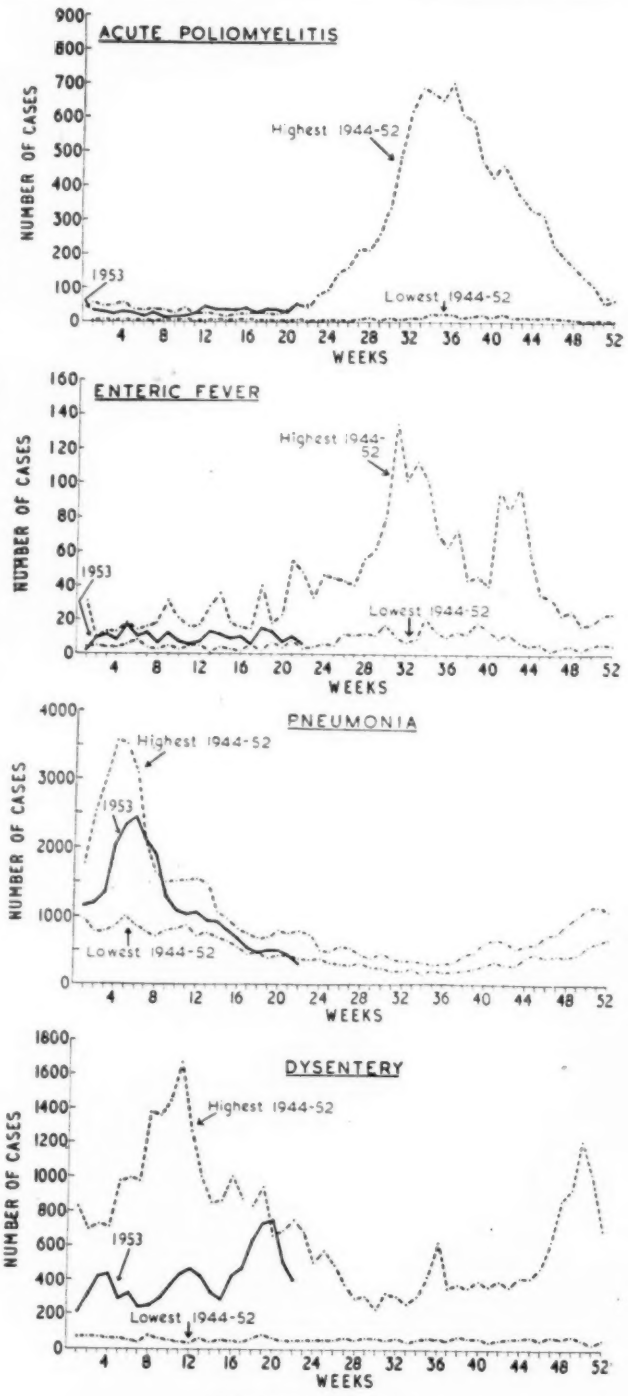
Thanks are due to Dr. S. C. Gawne, Lancashire county medical officer of health, for permission to supply these notes.

Week Ending June 13

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,055, whooping-cough 3,545, diphtheria 17, measles 7,532, acute poliomyelitis 73, dysentery 486, paratyphoid fever 5, and typhoid fever 6.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The incidence of infectious diseases fell in England and Wales during the week ending June 6. The falls in the number of notifications included 286 for measles, from 9,012 to 8,726; 326 for scarlet fever, from 1,084 to 758; 129 for acute pneumonia, from 446 to 317; 108 for dysentery, from 505 to 397; and 105 for whooping-cough, from 2,476 to 2,371.

The largest declines in the incidence of measles were 141 in Yorkshire West Riding, from 1,046 to 905, and 104 in Cornwall, from 305 to 201; while the largest rises were 168 in Surrey, from 132 to 300, and 94 in Lancashire, from 1,492 to 1,586. A small fall in the number of notifications of scarlet fever was recorded throughout the country; the largest declines were 35 in London, from 72 to 37, and 34 in Essex, from 75 to 41. The largest fluctuations in the returns of whooping-cough were falls of 68 in Lancashire,

from 277 to 209, 57 in Durham, from 130 to 73, and 50 in London, from 228 to 178, and a rise of 66 in Yorkshire West Riding, from 152 to 218. 10 cases of diphtheria were notified, 11 fewer than in the preceding week; this total was the lowest ever recorded, being 1 less than the previous lowest level.

51 cases of acute poliomyelitis were notified. These were 6 more for paralytic and 7 fewer for non-paralytic cases than in the preceding week. The cases are concentrated in the south of the country. 24 cases were notified in the south-eastern and south-western counties (excluding London), while only 8 cases were notified in the combined area of Yorkshire, north-western, and northern counties. During the past 10 weeks 386 cases have been notified, compared with 96 to 269 for the corresponding periods during the years 1947 to 1952. The largest returns during the week were Essex 5 (Southend-on-Sea C.B. 2, Ilford M.B. 2), Southampton county 5 (Bournemouth C.B. 5), Wiltshire 5 (Calne and Chippenham R.D. 3), Surrey 4, and Yorkshire West Riding 4.

The largest returns for dysentery were London 68 (Chelsea 13, St. Pancras 9), Middlesex 52 (Willesden M.B. 12, Edmonton M.B. 10), Lancashire 49 (Liverpool C.B. 16), Bedfordshire 35 (Luton M.B. 30), Durham 31 (Stanley U.D. 30), Yorkshire West Riding 24 (Leeds C.B. 11, Sheffield C.B. 9), and Leicestershire 21 (Leicester C.B. 21).

Medical News

First World Conference on Medical Education.—This conference will be held in London from August 22 to 29 this year under the auspices of the World Medical Association, with the collaboration of the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities. The president of the conference is Sir Lionel Whitby and the vice-president Professor W. Melville Arnott. The conference will meet in plenary session on Monday, August 24, when Sir Lionel Whitby will give his presidential address on "The Challenge to Medical Education in the Second Half of the Twentieth Century." There will then be addresses by Sir Richard Livingstone on "What is Education?"; by Professor John F. Fulton on "The History of Medical Education"; and by Colonel S. M. K. Mallick on "Medicine—a Technology or a Profession?" During the rest of the week the work of the conference will be done in the following four sections: (1) "Requirements for Entry into Medical Schools": vice-president, Dr. Victor Johnson, of the Mayo Foundation; rapporteur, Dr. Raymond Whitehead. (2) "Aims and Content of the Medical Curriculum": vice-president, Sir A. L. Mudaliar, of the University of Madras; rapporteur, Dr. A. Morgan Jones. (3) "Techniques and Methods of Medical Education": vice-president, Dr. A. Hurtado, of San Marcos University, Lima, Peru; rapporteur, Professor Ian Aird. (4) "Preventive and Social Medicine": vice-president, Professor René Sand, of the Université Libre, Brussels; rapporteur, Dr. Charles Fletcher. The conference is open to all interested in its work. A registration fee of £4 gives entry to all the sessions and to the excursions and entertainments in connexion with the conference. Early registration is advisable so that places in the excursions may be obtained; the registration bureau will also be opened on Saturday, August 22, on the night of which the B.M.A. Council, acting as the host organization of the conference, will give a reception. The sections will meet in B.M.A. House and the Friends House, Euston Road. Application for registration should be made to Dr. E. Grey Turner, secretary of the local arrangements committee, B.M.A. House, Tavistock Square, London, W.C.1. Communications on the programme of the conference should be addressed to Dr. Hugh Clegg, secretary of the programme committee, *British Medical Journal*, B.M.A. House.

The Lister Institute.—An impressive description of work in progress occupies the greater part of the annual report of the governing body of the Lister Institute of Preventive Medicine, the director of which is Dr. A. A. Miles. The studies carried on at the Institute are divided into three main groups: (*a*) bacteriological, immunological, and pathological; (*b*) biochemical; and (*c*) biophysical and physicochemical. The Institute also houses the blood group research unit and the blood group reference laboratory of the Medical Research Council. In concluding the report, Sir Henry Dale, O.M., chairman of the governing body, writes of the growing output of important and distinguished work from the different departments of the Institute, and continues: "Such a healthy growth of activities in a period of steeply rising costs inevitably gives cause for some anxiety on financial grounds; but the governing body will explore every possible source of such additional revenue as may be needed to meet any proper development."

"Family Doctor."—An article by Dr. J. A. Hadfield entitled "Is Punishment the Answer?" a profile of an M.O.H., and some facts about sunshine are included in the July issue of *Family Doctor*, which is now out. Other contributions include an article about summer diet, a first-hand account of having a spinal anaesthetic by Harry Cooper, some instructions on life-saving methods, and factual information about contact lenses. Robert T. Lewis has something useful to say about children's comics, and Roger Pilkington contributes another part to the series "How Your Life Began." Seasonable contributions include suggestions for the enjoyment of holidays free from the misery of travel sickness, methods for discouraging germs and flies, as well as a description of animal life on the sea-shore.

Tissue Transplantation.—At recent conferences in London and New York workers in plastic surgery, cancer, zoology, and other fields discussed common problems in tissue transplantation, and in the U.S.A. efforts to increase the exchange of information on this subject have culminated in a proposal to issue a quarterly *Transplantation Bulletin*. This will maintain, and publish at least once a year, a register of all medical practitioners and research workers interested in transplantation problems. The register will cover the fields of plastic surgery, endocrinology, cancer, genetics, immunology, experimental morphology, etc., and will be international in scope. The *Bulletin* will provide a medium for exchange of information and will maintain a bibliography covering the various branches of the subject, but will not publish formal papers. Those interested are invited to send their names and fields of interest to Dr. E. J. Eichwald, University of Utah College of Medicine, Salt Lake City, Utah, U.S.A. The subscription fee to cover cost of the *Transplantation Bulletin* and maintenance of the register and bibliography is $3, payable after the first issue of the *Bulletin*, which is expected in August, 1953.

Poliomyelitis Research in Scotland—Two units are to be established in Glasgow for the investigation of cases of poliomyelitis with respiratory paralysis. In addition workers at a special laboratory at the Ruchill Hospital are to study the poliomyelitis virus and the types occurring in Scotland. The Advisory Committee on Medical Research and the Medical Research Council will co-operate with the Western Regional Hospital Board in this research work.

Edward VI and St. Thomas's Hospital.—The charter refounding St. Thomas's Hospital, Bridewell, and Christ's Hospital was granted by Edward VI on June 26, 1553, ten days before his death. To mark the quatercentenary of this event, St. Thomas's is to hold a banquet at the Hospital's sports ground at Stoke d'Abernon on July 4.

Dr. J. O. Irwin has been awarded the Guy Medal in Silver by the council of the Royal Statistical Society in recognition of his contributions to statistical methodology, particularly in the field of bio-assay. Since 1948 Dr. Irwin has been editor-in-chief of Series B of the *Journal of the Royal Statistical Society*.

COMING EVENTS

Contraceptive Technique.—A lecture and demonstration on contraceptive technique will be given by Dr. Marie Stopes, Ph.D., at the Mothers' Clinic, 108, Whitfield Street, London, W.1, on Thursday, July 2, at 2.30 p.m. No fee is charged, but tickets must be obtained in advance.

Royal Medico-Psychological Association.—The annual meeting of this association will be held at Barnwood House, Gloucester, from July 7 to 10, under the presidency of Dr. G. W. T. H. Fleming. The annual dinner will be held at Barnwood House on July 8 at 7.30 p.m. Further information may be obtained from the secretary, R.M.P.A., 11, Chandos Street, Cavendish Square, London, W.1.

NEW ISSUES

Archives of Disease in Childhood.—The next issue (Vol. 28, No. 139) will be available in a week's time. The contents include:

TESTS FOR THE ADULTERATION OF HUMAN MILK. R. A. Miller and R. W. B. Ellis.
PULMONARY ATELECTASIS IN YOUNG CHILDREN. Margaret Griffiths.
ATYPICAL PNEUMONIAS IN CEYLONESE CHILDREN. C. C. de Silva and G. H. Cooray.
RECURRENT PAROTITIS IN CHILDREN. H. Everley Jones.
PULMONARY THROMBOSIS AND ITS ASSOCIATION WITH UNEXPECTED DEATH IN CHILDHOOD. John L. Emery.
BLOOD SUGAR STUDIES ON PREMATURE BABIES. O. Conor Ward.
INTRACRANIAL BRUITS IN INFANTS AND CHILDREN. Robert Hughes and R. McLaren Todd.
RUPTURE OF THE FOETAL HEART DURING LABOUR. R. A. McInroy and Anne L. M. Graham.
VASCULAR RING: A CAUSE OF CONGENITAL STRIDOR. Richard W. Smithells.
CONGENITAL STIPPLED EPIPHYSES. J. N. Briggs, J. L. Emery, and R. S. Illingworth.
INCREASED HAEMATURIA IN NEPHRITIS DURING CORTISONE AND A.C.T.H. ADMINISTRATION. L. Michaels and G. Walters.
HYPERPYREXIA IN THE POST-KERNICTERUS SYNDROME. W. H. Patterson and R. M. Forrester.
HODGKIN'S DISEASE IN CHILDHOOD. Donald M. Douglas and Albert E. Claireaux.
SOME SOCIAL AND ETHNIC VARIATIONS IN THE PHYSIQUE OF SOUTH AFRICAN NURSERY SCHOOL CHILDREN. H. T. Phillips.
A HISTORY OF INFANT FEEDING: PART II. SEVENTEENTH AND EIGHTEENTH CENTURIES. Ian G. Wickes.

Issued six times a year; annual subscription £3 3s., single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, June 29

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Colonel W. R. M. Drew, R.A.M.C.: Recognition and Treatment of Dysentery.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Arnott Demonstration by Dr. F. Stansfield: Paranasal Sinuses.
ROYAL EYE HOSPITAL.—5 p.m., Mr. R. A. Burn: Ophthalmic Problems of the General Practitioner.
UNIVERSITY COLLEGE.—At Physiology Theatre, 5 p.m., Dr. W. S. McCulloch (Massachusetts): Some New Techniques for the Electrophysiological Study of the Central Nervous System.

Tuesday, June 30

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. R. French: Medico-legal Problems and the Dermatologist.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Arnott Demonstration by Professor R. J. Last: Knee Joint.
ROYAL EYE HOSPITAL.—5 p.m., Mr. R. P. Crick: Ophthalmic Complications of Pregnancy and the Puerperium.

Wednesday, July 1

OXFORD UNIVERSITY.—At University Museum, 5 p.m., Litchfield Lecture by Professor Wilder Penfield, O.M., F.R.S.: The Learning of Languages—A Consideration of the Neurophysiological Mechanisms of Speech and Some Educational Consequences.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. E. F. Gale: Mode of Action of Antibacterial Agents.
YORKSHIRE SOCIETY OF ANAESTHETISTS.—At Leeds General Infirmary, 8 p.m., Symposium arranged by D. T. C. Gray: Facts about Dosage; opening speakers, Dr. J. W. Dundee, Thiopentone; Mr. H. F. V. Riddle, Nitrous Oxide; Dr. T. C. Gray, Relaxants.

Thursday, July 2

EMPIRE RHEUMATISM COUNCIL.—At Royal Society of Medicine, 8.15 p.m., Special Coronation Lecture by Sir Henry Cohen: Concept of Collagen Disease.
●HAMPSTEAD GENERAL HOSPITAL.—3 p.m., Dr. Harold Davis: Bleeding Peptic Ulcer; 4.15 p.m., Brains Trust.
INSTITUTE OF CHILD HEALTH.—5 p.m., Professor G. Fanconi (Zurich): Renal Dwarfism.
OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Professor W. B. Castle (Harvard): Speculations About the Cause of Polycythaemia Vera.
ROYAL COLLEGE OF SURGEONS OF ENGLAND AND INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—At Lincoln's Inn Fields, W.C., 5.30 p.m., Otolaryngology Lecture by Sir Henry Dale, O.M., F.R.S.: Histamine and its Antagonists.

Friday, July 3

INSTITUTE OF NEUROLOGY.—5 p.m., Professor Warren McCulloch: Cerebral Control of Carbohydrate Metabolism.

APPOINTMENTS

EDWARDS, J. R. G., M.B., B.S., F.R.C.S., Senior Registrar in Plastic Surgery Service of Newcastle-upon-Tyne Regional Hospital Board.

FARQUHAR, JOHN BURNS, M.B., Ch.B., F.R.C.S., M.R.C.O.G., Part-time Consultant Surgeon in Obstetrics and Gynaecology to the United Leeds Hospitals and to other hospitals in the Leeds district under the control of the Leeds Regional Hospital Board.

GLENN, ROBERT, M.B., B.Ch., D.P.H., Medical Officer of Health, School Medical Officer, and Port Medical Officer, Grimsby.

GUYMER, R. F., M.D., D.P.H., D.I.H., Part-time Lecturer in Occupational Health, St. Bartholomew's Hospital Medical College, and Chief Medical Officer to Lloyds Bank, Ltd.

HAY, ARTHUR WILLIAM, M.B., B.S., D.P.H., Deputy Medical Officer of Health, County Borough of East Ham.

HILL, J. NORMAN, M.B., Ch.B., D.P.H., Medical Director, Mass Miniature Radiography Unit based on St. James's Hospital, Leeds.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—Joseph Luder, M.D., M.R.C.P., D.C.H., Medical Registrar and Pathologist; M. J. Simpkiss, M.B., Ch.B., M.R.C.P., Assistant Medical Registrar; Doreen B. Pallot, M.B., B.S., D.A., Junior Resident Anaesthetist; F. L. Richardson, M.B., Ch.B., and Joan M. Wagner, M.B., Ch.B., M.R.C.P., House-physicians; F. C. Hoyte, M.B., B.S., House-surgeon to Orthopaedic and Plastic Departments; D. L. B. Farley, M.B., B.S., F.R.C.S., Surgical Registrar.

LAWSON, JAMES GLEN, M.B., Ch.B., M.R.C.O.G., Lecturer in Obstetrics and Gynaecology, University of Aberdeen.

LEDINGHAM, LESLIE ANDREWS, M.B., Ch.B., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Northern Regional Hospital Board, Inverness.

LIVERPOOL REGIONAL HOSPITAL BOARD.—G. J. Harrison, L.R.C.P.&S.I., D.P.M., Medical Superintendent (Consultant) to Winwick Hospital; J. Winter, M.B., Ch.B., M.Rad., D.M.R.D., Consultant Radiologist to Mill Road, Newsham General, and Bootle Hospitals; R. Marcus, M.D., Ch.M., F.R.C.S., Whole-time Assistant Consultant General Surgeon to Hospitals in Central Wirral area; L. Couper, M.B., Ch.B., D.P.M., Whole-time Deputy Medical Superintendent (Consultant) to Winwick Hospital; J. Winter, M.B., Ch.B., D.M.R.D., M.Rad., Consultant Radiologist to North Liverpool and Fazakerley Groups of Hospitals.

LYONS, SAMUEL E. C., M.B., B.Ch., D.P.H., Medical Officer to Strabane Hospital, Co. Tyrone, Northern Ireland.

MURDOCK, JAMES RONALD, M.D., D.P.H., D.C.H., Medical Officer of Health and Chief School Medical Officer, County Borough of Huddersfield.

WEIR, IAN B. L., B.Sc., M.B., Ch.B., D.P.H., D.P.A., Medical Officer of Health for the City of Dundee.

WHITEHEAD, J. P. S., M.R.C.S., L.R.C.P., Assistant Pathologist (S.H.M.O.), Scarborough, Whitby, Bridlington, and Malton Group Hospital Management Committee.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Allbrook.—On June 11, 1953, at the Mengo Hospital, Kampala, Uganda, to Mary, wife of Dr. David B. Allbrook, a brother for Roland—Malcolm Oliver Frith.

Clark.—On June 13, 1953, at Aberdeen, to Constance (formerly Eames), wife of Norman S. Clark, M.B., M.R.C.P., D.C.H., a son.

Khosla.—On May 31, 1953, at the West Middlesex Hospital, Isleworth, Middlesex, to Saroj, wife of Dr. H. Khosla, a son—Rajiv.

Langford.—On June 15, 1953, at British Military Hospital, Hamburg, B.A.O.R., 3, to Lois, wife of Colonel R. C. Langford, A.D.M.S., Hamburg District, a daughter.

MARRIAGES

Chovil—Béland.—On June 26, 1953, in Paris, France, Alan Chovil, M.B., B.Chir., of Fareham, Hants, to Mariella Béland, of Quebec, Canada.

DEATHS

Boyd.—On May 19, 1953, at his home, Mount Side, Ilsham Valley Road, Torquay, George Samuel James Boyd, M.R.C.S., L.R.C.P., late of Four Oaks, Sutton Coldfield, Warwicks.

Cran.—On June 1, 1953, at Grassington Lodge, Dorking, Surrey, Hugh Rose Cran, M.R.C.S., L.R.C.P., late of New Malden, Surrey, aged 75.

Grieve.—On May 30, 1953, at Fontainebleau, France, Stewart Cameron Cavers Grieve, M.B., Ch.B., Flying Officer, R.A.F., of 8, Meadowbank View, Kirknewton, Midlothian.

Harry.—On May 25, 1953, at his home, Dolebury House, Churchill, Somerset, Philip Anthony Harry, M.D., D.P.H., formerly of Rochdale, Lancs.

Kessler.—On May 9, 1953, in a London Hospital, Denys Edward Kessler, M.R.C.S., L.R.C.P., of Windwhistle, Ringwood, Hants.

Lawlor.—On May 12, 1953, at King's College Hospital, London, S.E., Geoffrey Leo Thomas Lawlor, L.M.S.S.A., of 133, Camberwell New Road, London, S.E., aged 69.

Macbeth.—On May 9, 1953, Alison Nicol Macbeth, M.B., B.S., aged 56.

Macbride.—On April 1, 1953, Henry John Macbride, M.D., of 103, Embassy Court, Brighton, Sussex, formerly of London, W., aged 60.

McCall.—On May 6, 1953, in a nursing-home, James McIntosh McCall, M.B., C.M., M.R.C.V.S., late of Chalfont St. Giles, Bucks, aged 87.

McEwan.—On May 26, 1953, at Nakuru, Kenya, George Clazy McEwan, M.B., Ch.B., D.P.H.

Mackay.—On April 26, 1953, in Melbourne, Australia, Charles Vincent Mackay, M.D., F.R.A.C.P.

McNaughton.—On May 16, 1953, at Lushoto, Tanganyika, James Garvie McNaughton, M.D., M.R.C.P.Ed.

Main.—On May 14, 1953, William Robert Main, M.B., Ch.B., of the Garden House, Buckingham.

Nicoll.—On May 13, 1953, in a hospital, Exeter, George Stalker Nicoll, M.B., Ch.B., of Low Barlay, Gatehouse-of-Fleet, Castle Douglas, Kirkcudbright.

Smith.—On May 22, 1953, at Tunbridge Wells, Kent, Mary Anne Smith, L.R.C.P.&S.Ed., L.R.F.P.S., aged 90.

Speirs.—On May 11, 1953, at his home, Furze Bank, Diss, Norfolk, Hugh Meredith Speirs, M.D., aged 75.

Style.—On May 23, 1953, at Hadleigh, Suffolk, Arthur Hurrell Style, M.D., aged 79.

Walker.—On May 23, 1953, at St. Thomas's Hospital, Hydestile, Surrey, Norman Dunbar Walker, O.B.E., M.B., Ch.B., D.P.H., Lieutenant-Colonel, R.A.M.C., retired, aged 76.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Long-standing Warts

Q.—*What is the best treatment for long-standing (five years) warts on the arm of a woman?*

A.—The most suitable treatment of a crop of common warts on the arm depends to some extent on the number of warts present. If there are not more than half a dozen it will probably be best to treat them individually by freezing with carbon-dioxide snow. Treatment should be sufficient to raise a blister, and, in this situation, 30 to 45 seconds with firm pressure will probably be suitable. If the warts are very numerous it may be better to remove them with the curette. This is not at all difficult, but seems to require a knack of scraping off the warts completely and smoothly in the right plane. Preliminary freezing with an ethyl-chloride spray provides fairly good analgesia, but in nervous patients a short general anaesthesia may be best. After curettage, the areas should be covered with a dry dressing, which is left in place, and kept dry for a week or 10 days. The areas should not be completely occluded with "elastoplast." At the end of 10 days they will be healed, and if curettage has been complete recurrence is not very likely.

Cartridge Syringes

Q.—*Certain syringes in which disposable cartridges are used preclude aspiration of blood before injection. The syringes are obviously convenient, but do the dangers from not being able to tell if a vein has been entered make them unsafe for use in domiciliary practice?*

A.—These syringes are convenient, and for most purposes quite satisfactory, despite the objection referred to in the question. On the other hand, when the medicament to be injected is one that can cause untoward effects if it enters a vein, it would seem advisable to use another type of syringe. Among such medicaments are suspensions in oils, and preparations of procaine and other newer forms of penicillin, the accidental intravenous injection of which is believed to have caused serious effects. It would likewise be unsatisfactory to use these syringes for the intravenous injection of drugs which cause local damage when they escape into the tissues.

Vitamin B_{12} in Pernicious Anaemia

Q.—*As a pernicious anaemia patient receiving 50 μg. of vitamin B_{12} fortnightly and feeling perfectly fit, I often wonder how this microscopical amount of intramuscular B_{12} meets up with the non-existent intrinsic factor from my achylic stomach. The greater would be my wonder had I suffered total gastrectomy. The latest writers on haematology concur in agreeing that pernicious anaemia only rarely follows total gastrectomy. There certainly can be no intrinsic factor in a non-existent stomach. Can you please explain this to me?*

A.—In a normal person Castle's extrinsic factor, which is now thought to be identical with vitamin B_{12}, combines with an intrinsic factor present in gastric juice and enters the epithelial cells of the small intestine. Here it is bound with another substance and passes to the liver to be stored. The person suffering from pernicious anaemia lacks intrinsic factor, and so fails to absorb the minimum amount of vitamin B_{12} necessary for the normal maturation of red cells. The average diet in this country contains about 5 μg. of vitamin B_{12}, much of which is not absorbed even by the normal person, and this explains why the average amount by injection of 3 μg. a day required by the patient with pernicious anaemia is so small.

Total gastrectomy is usually performed for carcinoma of the stomach, and many such patients do not survive long enough to develop a megaloblastic anaemia. In those that do survive, anaemia is not uncommon. Thus, of 53 cases surviving for more than three years, 12 had developed macrocytic anaemia and 5 an anaemia of doubtful nature; only 10 of the remainder had definitely received no liver therapy.[1] It seems probable that intrinsic factor may be present in the duodenal mucosa[2] of some normal individuals, and that in patients with pernicious anaemia atrophy of the glands producing intrinsic factor is not confined to the stomach. The question is fully discussed by Conway and Conway.[3]

REFERENCES

1 Macdonald, R. M., Ingelfinger, F. J., and Belding, H. W. (1947). *New Engl. J. Med.*, 237, 887.
2 Bethell, F. H., Meyers, M. C., Andrews, G. A., Swendseid, M. E., Bird, O. D., and Brown, R. A. (1947). *J. Lab. clin. Med.*, 32, 3.
3 Conway, N. S., and Conway, H. (1951). *British Medical Journal*, 1, 158.

Herpes Zoster and Chicken-pox

Q.—*Is it established that an attack of herpes zoster in a child will result in immunity to chicken-pox? If so, is the immunity invariable and lasting?*

A.—This is a difficult question to answer outright—unless perhaps by saying simply, so far as the first part of the question is concerned, that it has not been established; there is, indeed, no evidence one way or the other that an attack of zoster may result in immunity to chicken-pox. The two infections are, of course, due to the same or closely related viruses. Second attacks of either disease are rare. But chicken-pox does not prevent the development of zoster in later life, possibly, it has been suggested, because zoster results from the reactivation of virus which has remained latent within the body since the original attack of chicken-pox. The collection of adequate evidence in the reverse direction is rendered difficult because chicken-pox is predominantly a disease of childhood, whereas zoster is more frequently encountered in adults.

Ergometrine for Retained Placenta

Q.—*Is it a good thing to give intravenous ergometrine when there is a retained placenta?*

A.—The use of ergometrine in cases of retained placenta depends very much on the circumstances of the case. If, in addition to retention of the placenta, there is also haemorrhage, and if the attendant is working under conditions of domiciliary practice, then 0.5 mg. ergometrine should be injected intravenously without hesitation. This may or may not be followed by delivery of the placenta, but it will almost certainly control the bleeding. The advantage is that, even if the placenta remains in the uterus, the immediate threat to life is arrested, and the attendant has time to obtain assistance and to make proper preparations for manual removal of the placenta to be carried out as a planned operation.

If the placenta is retained but no haemorrhage is taking place, opinions and practice vary. If the patient is in hospital with all facilities at hand there is much to be said for manual removal of the placenta, delaying the intravenous injection of ergometrine until the moment the placenta is withdrawn. The same is true for domiciliary practice, provided help can be obtained for carrying out the operation without undue delay. There may be circumstances, however, in which ergometrine can be given with advantage, for it may lead to expulsion of the placenta, or promote its separation so it can be expressed. If it fails, however, the placenta still has to be removed manually, and this operation may then be rather more difficult because of uterine spasm. Nevertheless, this difficulty tends to be overrated.

Absence of Axillary Hair in a Man

Q.—*An athletic young man of 18 suffers considerable embarrassment when changing with other men, as he has no axillary hair and a feminine distribution of his pubic hair. He does not need to shave. His genitalia are normally developed, and he has heterosexual interests. What are the likely causes of this condition, and what treatment is advised?*

A.—The usual cause of failure of growth of sexual hair is deficient secretion of testosterone by the interstitial tissue of the testes. On the other hand, it may sometimes be due to resistance of the hair follicles to the normal stimulation of testosterone. This latter cause is probable in the present case, since the patient's genitalia are normally developed. If this is so, there is no effective treatment. However, I suggest that a trial be made with testosterone propionate injected intramuscularly in doses of 50 mg. twice a week. Several months' treatment will be necessary. If injections prove to be inconvenient, methyl testosterone may be given by mouth in doses of 25 mg. daily.

Barrier Creams for Oily Materials

Q.—*What barrier creams are useful against oily materials in industry?*

A.—Various creams have been advocated as protection against oily materials in industry, but objective laboratory tests[1] have shown that they are penetrated, even when liberally applied, by cutting oils within three-quarters of an hour. The most effective type of cream consists of soap, inert filling powder, and water with small amounts of glycerin; such mixtures certainly facilitate removal of grease and dirt from the hands—for example, of car repairers. But daily application of soapy creams is probably undesirable on many skins. In general, hygienic measures such as good washing facilities and suitable cleansers are more likely to be valuable. The emollient cream of anhydrous lanolin (65 parts) and castor oil (35 parts) described in an earlier question[2] also assists washing and skin protection.

REFERENCES

1 Cruickshank, C. N. D. (1948). *Brit. J. industr. Med.*, **5**, 204.
2 *British Medical Journal*, 1952, **2**, 1058.

Castellani's Paint and Myxoedema

Q.—*Is there any chance of the resorcinol in Castellani's paint (pig. magent., N.F.) being absorbed through the skin and having an anti-thyroid effect? The paint contains 8% resorcinol. I am using it for recurrent fungus infection of the skin, and treatment may well be prolonged, say, up to a year.*

A.—Resorcinol has been shown to be capable of producing myxoedema when applied to varicose ulcers of the leg. In the recorded cases the patients all had large open ulcers, and the ointment had been applied for a long time. It is, however, possible to affect thyroid function if resorcinol is applied to unbroken skin for a sufficiently long time. It seems unlikely that a fungus infection would affect a sufficiently large area of skin to cause a significant risk of myxoedema from the application of 8% resorcinol as a paint. Nevertheless, it would be advisable to keep the possibility in mind, and to note particularly any alteration in tolerance to cold, in the dryness of the skin, in the hair, or in the voice.

Prognosis of Orthostatic Albuminuria

Q.—*What is the long-term prognosis for a young man in whom, after full investigation in hospital, a diagnosis of orthostatic albuminuria has been made?*

A.—Orthostatic albuminuria is a benign condition; it may disappear spontaneously, and the long-term prognosis is excellent. It would be a wise precaution, however, to maintain contact with the patient for several years and check occasionally the amount of albumin in specimens passed at different times of the day.

NOTES AND COMMENTS

Oestrogens and Vasomotor Rhinitis.—Dr. J. PEPYS (London, S.E.1) writes: The observation of your correspondent on the beneficial effect of oestrogen treatment in a case of vasomotor rhinitis at the menopause ("Any Questions?" May 23, p. 1177) corresponds with that reported by Lucas and Pepys.[1] A very good response to oestrogen treatment was described in 39 women who developed rhinitis at or about the menopause, and a further eight similar cases have been seen by me since that time. These patients correspond in every way with other cases of typical allergic rhinitis, and present the same clinical history of sneezing, itching of the nose, nasal obstruction, and rhinorrhoea; the same nasal mucosal appearances; and the same response to oral administration of palliatives such as antihistaminic drugs or ephedrine. The nasal secretions frequently contain significant numbers of eosinophil cells, and skin testing and clinical trials support their histories, which suggested chiefly inhalant allergens. Treatment by oestrogens alone without any allergic treatment was effective in 33 cases, and six cases required both oestrogen and allergic treatment to obtain the best results. In these cases the response to oestrogens, either ethinyl oestradiol 0.05 mg. daily or stilboestrol 1 mg. daily, is rapid, often complete, and is contemporaneous with their administration. Cessation of treatment can lead to a recurrence of symptoms, which are rapidly controlled again on resumption. Treatment must be continued over a long period just as with the use of oestrogens for other menopausal symptoms, and the best time for tapering off the dosage varies from patient to patient. A similar response to oestrogen is occasionally found in female asthmatics at the menopause; in one case of severe intractable asthma a remarkably beneficial result was obtained. A possible explanation of this response to the oestrogen treatment is that the hormonal disturbance has lowered the clinical threshold and upset the "allergic equilibrium," thus enabling clinical manifestations to appear.

REFERENCE

J. Laryng., 1951, **65**, 598.

Spontaneous Combustion of Alcoholics.—Professor B. BRENDAN HICKEY (Khartum) writes: With reference to "Spontaneous Combustion of Alcoholics" in "Any Questions?" (*Journal*, April 4, p. 793) and the subsequent note by Dr. H. H. MacWilliam (*Journal*, April 18, p. 896), I should like to draw attention to a further account of the alleged occurrence in fiction. Captain Marryat in *Jacob Faithful* describes in a most dramatic fashion the death of Jacob's mother, a confirmed alcoholic who rarely ever left her bunk in a barge. Coming as this description does from so experienced an observer as Marryat, and coinciding so accurately with other descriptions, it is perhaps legitimate to conclude that combustion, spontaneous or otherwise, was seen not infrequently in obese alcoholics and occurred with the macabre features usually described.

[The account of this incident is to be found in Chapter 1 of *Jacob Faithful*. It reads as follows:

"Nothing was burning—not even the curtains to my mother's bed appeared to be singed. I was astonished—breathless with fear, with a trembling voice, I again called out 'Mother.' I remained more than a minute panting for breath, and then ventured to draw back the curtains of the bed—my mother was not there! but there appeared to be a black mass in the centre of the bed. I put my hand fearfully upon it—it was a sort of unctuous, pitchy cinder. . . .

"As the reader may be in some doubt as to the occasion of my mother's death, I must inform him that she perished in that very peculiar and dreadful manner, which does sometimes, although rarely, occur, to those who indulge in an immoderate use of spirituous liquors. Cases of this kind do indeed present themselves but once in a century, but the occurrence of them is but too well authenticated. She perished from what is termed *spontaneous combustion*, an inflammation of the gasses generated from the spirits absorbed into the system."]

Correction.—The outbreak of food-poisoning caused by the *danysz* variety of *Salm. enteritidis* mentioned in the reply to a question on "Dangerous Mouse Poisons" (May 30, p. 1233) occurred in 1951, and not in 1950 as stated in the answer.

All communications with regard to editorial business should be addressed to The EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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